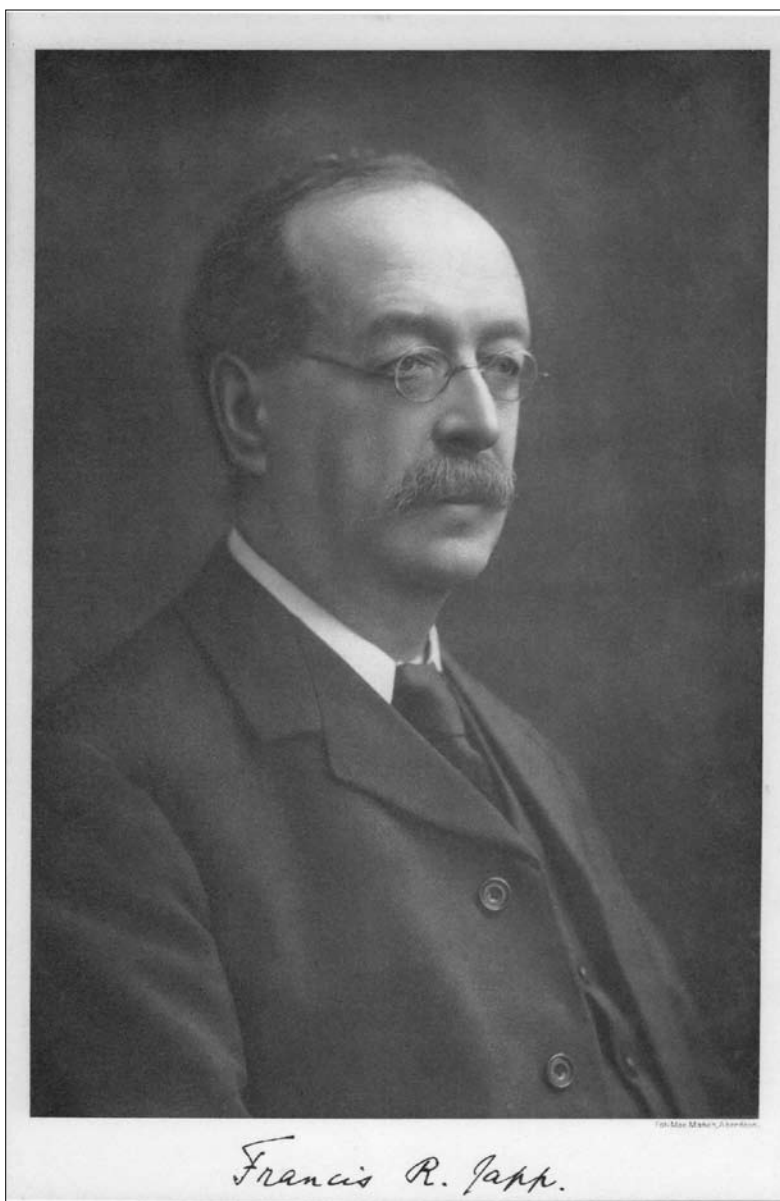


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LOST ARTIFACTS? [See p 111]

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ON THE DISCOVERY AND HISTORY OF PRUSSIAN BLUE

Alexander Kraft, Gesimat GmbH, Berlin

Introduction

In the early 18th century Prussian Blue (ferric hexacyanoferrate(II)), the first purely synthetic pigment, was discovered. This new blue pigment was less expensive and more readily available or more easily produced as compared to ultramarine or other blue pigments which were in use at the time as a blue color in paintings. Prussian Blue is a very stable compound with the exception of being labile in alkaline media. The discovery of Prussian Blue is still enigmatic and has not been well researched. Today, Prussian Blue is still used as a pigment, but it also has other applications ranging from electrochromics and sensors to poison antidotes.

The Conventional Story of the Discovery of Prussian Blue

Prussian Blue was first mentioned in the scientific literature in the first issue of the publication of the Royal Prussian Society of Sciences (Königlich Preussische Sozietät der Wissenschaften) (1) *The Miscellanea Berolinensia ad incrementum Scientiarum* in 1710 (2). (A German translation of this Latin text was subsequently published (3)). This first written account of Prussian Blue was published anonymously (the author was most probably Johann Leonhard Frisch as will be discussed below). This early report revealed almost nothing of the discovery of Prussian Blue nor did it give a method for the preparation of the pigment. Rather, it was a kind of

advertisement for the new material under the auspices of the new scientific society, and it was stated that Prussian Blue could be bought from the book dealers of the society.

The conventional story of the invention of Prussian Blue was told by Georg Ernst Stahl (1660-1734) (4) in a book he published in 1731 (5). In this book, published about 25 years after the discovery of Prussian Blue, Stahl reported 300 experiments supporting the phlogiston theory of oxidation and combustion. As related by Stahl (5), the discovery of Prussian Blue (Stahl writes "Caeruleum Berolinense") took place in Berlin in the laboratory of Dippel ("Dippelius"), although no date was given. Dippel was preparing so-called animal oil ("oleum animale") by distillation of animal blood to which potash (potassium carbonate, or as Stahl writes "Sale tartari") was added. Concurrently, a color maker named Diesbach was working in Dippel's laboratory. Diesbach was attempting to produce Florentine lake, a red pigment based on cochineal red. Usually he did this by precipitation of an extract of cochineal (produced by boiling dried cochineal insects with water to extract the carminic acid) with alum ($KAl(SO_4)_2 \cdot 12H_2O$), iron sulfate ("Vitrioli Martialis"), and potash ("Sale alcalico Tartari"). However, having no more potash, he borrowed some from Dippel that had been used in his animal oil production. This potash was contaminated with hexacyanoferrate; and therefore the addition of contaminated potash to the solution, which already contained iron

sulfate, resulted in a blue precipitate, the Prussian Blue, instead of the expected red product.

To date, these two reports (2, 5) have been considered to be the only sources of information on the very early history of Prussian Blue. However, there exists a neglected source of information on the first years of Prussian Blue: the correspondence of Leibniz.

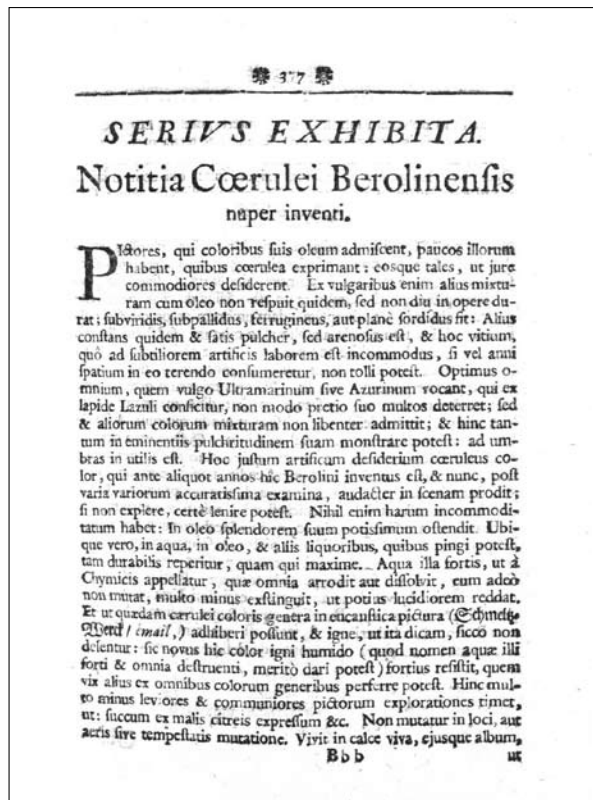


Figure. First page of the first publication on Prussian Blue from the *Miscellanea Berolinensia ad incrementum Scientiarum* (2)

The Correspondence of Leibniz

Gottfried Wilhelm Leibniz corresponded with an enormous network of people scattered throughout Europe. This correspondence was conducted in several languages, mainly in Latin, French, and German (6).

A major additional source on the very early history of Prussian Blue is a set of letters sent from Johann Leonhard Frisch (1666-1743) in Berlin to Gottfried Wilhelm Leibniz in Hannover (7), which were first published in a book in 1896 (8). This book contained 37 letters from Frisch to Leibniz between the end of 1706 and September 19, 1716 (Leibniz died on November 14, 1716), together

with three responses from Leibniz to Frisch. Thirteen of these letters from Frisch mention the new pigment Prussian Blue; and in five letters Diesbach, one of two inventors indicated by Stahl (5), is mentioned (Frisch writes his name “Diessbach” or “Dieszbach”). Diesbach is mentioned in direct connection with the new blue color. The letters do not state the first name of Diesbach, the story of the invention of Prussian Blue, or the names of the inventors.

Johann Leonhard Frisch had been living in Berlin since 1698. He taught at the Berlin Gymnasium located in the former Grey Monastery of the Franciscans. Frisch had been a member of the Berlin Society of Sciences since 1706 (8). In his first letter to Leibniz in which Prussian Blue is mentioned, written on March 31, 1708, Frisch informed Leibniz that he had already earned some money with his blue color. In the second letter that mentions Prussian Blue, dated April 28, 1708, Frisch stated that he had made the color better than the original inventor had done and that the production process was now less expensive.

In a much later letter of September 14, 1715, however, Frisch informed Leibniz that he himself was the inventor. This statement may have been a reaction to an assertion made to Leibniz by Diesbach’s father-in-law Müller (at this time residing in Vienna), who claimed to be the inventor of Prussian Blue. This letter also clarified that the secret of the production of Prussian Blue was strongly protected and that at this time (in 1715), at least in Berlin, only Diesbach and Frisch knew how to make Prussian Blue. (The name of Dippel, the second possible original inventor, did not appear in the letters from Frisch to Leibniz).

The name Prussian Blue (“Preussisch-blau”) is used in one letter dated August 25, 1709 and the name Berlin Blue (“Berlinisch Blau” or “Berlin Blau”) in two later letters (from November 9, 1709 and September 2, 1712). However, in most letters, it was simply called the blue color (“blaue Farb(e)”). The name of Diesbach appears for the first time in a letter from September 28, 1709, which stated that Diesbach had printed an informational sheet for painters about the blue color.

Diesbach seems to have been active in alchemical studies as well. Indications of these investigations appeared in two letters (from September 28, 1709 and undated, but perhaps from about spring 1710).

In a letter of November 9, 1709, Frisch sent Leibniz a Latin text about the blue color. In another letter from January 30, 1710, he told Leibniz that the text “*notitia*

caerulei Berolinensis" that Leibniz sent back had been added to the texts for the *Miscellanea*. These two letters most probably refer to the first publication on Prussian Blue (2). It appears that Frisch was the author of this publication which had been published anonymously.

The profitable business of selling Prussian Blue was cause to protect the secret of its preparation. In several letters to Leibniz Frisch revealed details of his commercial success with selling Prussian Blue. At that time, Diesbach was producing Prussian Blue while Frisch was selling it, at least outside Berlin. In a letter dated October 29, 1712, Frisch wrote that he was not able to satisfy the demand for Prussian Blue. Soon imitation Prussian Blue, perhaps indigo blue being sold as Prussian Blue, appeared on the market (letter from August 25, 1709).

Because of the large amount of money Frisch earned by selling Prussian Blue, he was able to buy land outside the Spandau Gate of Berlin. He used this land for his botanical experiments with mulberry trees and other plants, according to a letter from July 26, 1715. As an example of his sales, this letter indicated that he sold 100 pounds of Prussian Blue in Paris for 30 thaler per pound in the year 1714.

Sales of Prussian Blue that were explicitly described included those to Wolffenbüttel (9) (letters from September 28, 1709 and November 9, 1709), in Paris (letters from July 26, 1715 and September 19, 1716) and in St. Petersburg (letter from September 19, 1716). In the last of these letters, Frisch reported to Leibniz that in Paris two factories that produced ultramarine (10) ("Outremer") had been closed because of the large amounts of Prussian Blue he delivered to Paris.

Leibniz was obviously somewhat involved in the sale of Prussian Blue or at least was active in informing potential customers about this new pigment. Frisch wrote Leibniz in a letter dated September 2, 1712, that Bernoulli (a Swiss mathematician from Basel who corresponded with Leibniz, see below) could purchase his half pound of Prussian Blue in Leipzig from Gleditsch for 15 thaler.

The only use of Prussian Blue reported in these letters is as a blue pigment for painters. The letter of September 28, 1709 reported that (Christoph Joseph) Werner (11), a Swiss painter in Berlin, had used the blue color for a long time and that he had sent it to other painters in quantity (8). Recently, Bartoll et al. (12) showed in an investigation of paintings from the collection of King Friedrich II of Prussia (the grandson of Friedrich I)

that Prussian Blue can be found in paintings from Watteau that were painted in Paris between 1710 and 1712. Prussian Blue was also detected in paintings produced in Berlin by Antoine Pesne and others, the earliest being from 1710 (12). However, the earliest painting in which Prussian Blue was identified by Bartoll and colleagues was the "Entombment of Christ" by the Dutch painter Pieter van der Werff (1666-1720), which was painted in 1709 in the Netherlands. As shown below, during this time Dippel lived in the Netherlands and was also producing Prussian Blue.

In addition to the Frisch letters, other correspondence of Leibniz referred to Prussian Blue. In his correspondence with Johann Bernoulli (1667-1748) between December, 1710 and December, 1711 (13), Prussian Blue was discussed. Another example is a letter from Paris (dated August 17, 1714), in which the writer Hasperg told Leibniz (14) that Homberg (15) wanted Leibniz to describe the procedure for production of Prussian Blue. This letter mentioned that Leibniz had previously written to Homberg about Prussian Blue. Hasperg also stated in this letter that he and Homberg did not know the identity of the inventor. He further told Leibniz that a German in the Netherlands with the name "Dipelius" was also preparing the blue color and that he had a sample of this color, which was not as beautiful as the blue color from Berlin. Thus, it is clear that during his stay in the Netherlands, Dippel, the second inventor indicated by Stahl (5), was also producing Prussian Blue, but of an inferior quality.

Dippel in Berlin and the Netherlands

According to Stahl (5), the invention of Prussian Blue took place in the laboratory of Johann Konrad Dippel (1673-1734) in Berlin. Documents from the period showed Dippel's name, variously written as Dippelio, Dipelius, or Dippelius. He was a theologian, alchemist, and physician. Many of his mostly theological books were printed under the pseudonym Christianus Democritus. (Further information on Dippel's life can be found in Ref. 16-18) (19).

Around 1700, after some years of theological dispute, Dippel became interested in alchemy. First, he concentrated on attempts to transmute base metals into gold and later turned to finding a universal medicine. He thought that a substance which he called animal oil, produced by destructive distillation of animal blood, would be this universal medicine. Aynsley and Campbell wrote of Dippel's animal oil (18):

A glance at the list of principal constituents is enough to convince one of the heroic nature of the cure.

In the autumn of 1704, he moved to Berlin, invited by Count August David zu Sayn-Wittgenstein (1663-1735), who was one of the leading figures at the court of King Friedrich I. Here he rented a palatial house for his alchemy studies. Johann Georg Rosenbach, also a radical pietist, was living in this house and took part in Dippel's experiments.

In the early 18th century, Berlin was a good environment for alchemists who claimed to be able to convert common metals into gold. However, if they were not able to deliver gold, it could become dangerous. Of the alchemists who were active at this time in Berlin, Johann Friedrich Böttger (1682-1719) and Domenico Emanuele Caetano (?-1709) are the most famous. In 1701 Böttger fled from Berlin to Saxony, where he was later involved in the invention of European porcelain. Caetano arrived in Berlin in 1705. Dippel participated in the first tests of the abilities of Caetano as an alchemist. In 1709 Caetano was hanged in Küstrin (20). Other alchemists active in Berlin at that time, mentioned by Frisch in his letters to Leibniz (8), included Felmi (or Felmy or Filmey) and Meder.

Nothing specific is known about the alchemistic work of Dippel in Berlin. In early 1707 Dippel was arrested and held for about a week in the Hausvogtey prison at the request of the Swedish ambassador. Dippel had published a new theological book, which contained some harsh criticism of the Swedish Lutheran church. He was released on bail provided by Count Wittgenstein and soon fled from Berlin to the Netherlands. Living in Maarsen between Utrecht and Amsterdam, he worked as a physician for the next few years. From the letter of Hasperg to Leibniz, written in 1714 (14), it can be concluded that Dippel was also producing Prussian Blue during his stay in the Netherlands. He left the Netherlands in 1714 (21).

Since Dippel arrived in Berlin in the autumn of 1704 and left Berlin early in the year 1707, the invention of Prussian Blue most probably took place in 1705 or 1706. In a handwritten Berlin chronicle from approximately 1730 (22), the invention of Prussian Blue by the Swiss "Joh. Jacob Diesbach" is recorded for the year 1706. This date is the most probable year that is based on original sources.

The Secret is Out

Despite the efforts to conceal the production method of Prussian Blue, it remained secret for only about 20 years. In 1724 John Woodward published a procedure for the production of this color in the *Philosophical Transactions of the Royal Society* in London (23), and it was immediately followed by an account of some detailed experimental work on Prussian Blue by John Brown (24) in the same issue. The Woodward paper was based on a letter sent to him from Germany that disclosed the heretofore secret procedure, but Woodward did not publish the name of the author. Brown, a Fellow of the Royal Society since 1721, stated in his paper that (24):

Dr. Woodward having lately communicated a paper (which he receiv'd from another hand) to this Society, containing a Process for making the Prussian Blue, I was willing to go thro' it exactly, according to the proportions there prescrib'd.

Obviously, John Woodward (1657-1728) (25), a physician, naturalist, and geologist, had asked the chemist Brown (?-1735) to perform some preliminary experiments to verify the contents of the paper he had received from Germany. In January / February, 1724 these two papers (23, 24) were communicated to the Royal Society and printed in the *Transactions*.

In his experiments Brown (24) not only followed the method communicated by Woodward, but also varied the procedure by precipitation of alternative metal hexacyanoferrate compounds, using silver, mercury, copper, bismuth (denoted as "Tin-Glass"), and lead instead of the iron used for preparing Prussian Blue. Thus, he performed the first documented research on the so-called Prussian Blue analogs, which continue to represent a major research field today. However, these experiments did not result in the beautiful blue precipitate that iron hexacyanoferrate gave. He also showed that in the calcination step, animal blood could be replaced by flesh ("beef") during the production process of Prussian Blue.

From whom Woodward received the information for making Prussian Blue is not clear and remains open to further investigation. Shortly after the two publications of Woodward and Brown, other people repeated the experiments and came to additional new conclusions. Notably Etienne-Francois Geoffroy (1672-1731) (26) in 1725 communicated to the French chemists the secret of the Prussian Blue production and published some new information (27-29). He found that Prussian Blue production could be achieved from other parts of

animals such as horn, hair, skin, or hoof, in addition to dried blood and flesh (28).

With the secret of its preparation revealed, production of Prussian Blue began throughout Europe. Often it was sold under different names such as Paris Blue or Milori Blue, usually named after the production location, the owner of the facility, or based on an advertising idea (30). The production technology changed greatly over time. Asai analyzed about 100 methods published between 1724 and 1904 and documented the increasing improvements in product quality that resulted (30).

Prussian Blue was not only used as a pigment for painters but it was soon applied to the dyeing of textiles, following the work of P. J. Macquer (1718-1784) (31) conducted in 1749 toward this goal (32). Prussian Blue was also used for blueing textiles, is still used as a pigment today, and sold under the commercial name Iron Blue.

The Continuing Story of Prussian Blue

Starting in 1724 and continuing for about 250 years, chemists tried to define the composition, stoichiometry, and structure for Prussian Blue. Eminent scientists such as Priestley, Scheele, Berthollet, Gay-Lussac, and Berzelius were among the researchers in the field (33). In 1782 Scheele discovered hydrogen cyanide by heating Prussian Blue with diluted sulfuric acid (34), and in 1811 Gay-Lussac's determination of the composition of hydrogen cyanide (35) led to the conclusion that Prussian Blue contained cyanide. Because of the lack of modern analytical methods, the details of the crystal structure and even of the analytical composition of Prussian Blue were for a long time only partially resolved.

The first structural hypothesis for Prussian Blue was presented by Keggin and Miles with the help of X-ray powder patterns (36). Finally, in the 1970s Ludi et al. (37) published a detailed structure and confirmed the composition as $\text{Fe}_4[\text{Fe}(\text{CN})_6]_3 \cdot x\text{H}_2\text{O}$ ($x = 14-16$), which is now accepted as correct.

The use of Prussian Blue as a painter's pigment in the early 18th century and as a dye for coloring textiles was followed by other uses. An important example is the cyanotype or blueprint process invented by Herschel in 1842 (38). This was a commercially successful photocopying process in use from 1843 until the early 1940s. Prussian Blue is also used in analytical applications, e.g., spot tests in the classical analytical chemistry of iron.

Prussian Blue has a very high affinity for thallium and cesium ions (39). Therefore, people who have become internally contaminated with radioactive thallium, nonradioactive thallium, or radioactive cesium can be treated by orally administered Prussian Blue, which traps thallium and/or cesium in the gut and thereby increases fecal excretion. Thus, the biological half-life of thallium and cesium is significantly reduced after capture therapy with Prussian Blue (39).

In 1978, Neff published a short notice in which he described the electrochemical deposition of thin films of Prussian Blue from aqueous precursor solutions onto conducting substrates. These films can be switched reversibly by electrochemical means between different colored oxidation states (40) in a process called electrochromism. Especially interesting for practical use is the alternation between colorless and blue oxidation states. One possible new application is the construction of so-called smart windows which can reversibly change their transmission of light between very high and low values (41).

Another technically interesting property of Prussian Blue is its ability to catalyze the reduction of hydrogen peroxide and molecular oxygen (42). Current investigation is underway to employ this effect for the construction of sensors for clinical, environmental, and food analysis (43). Prussian Blue also holds some potential as an active material in modern batteries (44) or as an electrocatalyst for fuel cells (45).

Conclusions

Prussian Blue was discovered by Diesbach and Dippel between 1704 and 1707, but most probably in 1706 in Berlin. Written evidence indicates that Prussian Blue was produced at least between 1708 and 1716 in Berlin by Diesbach and Frisch, and that it was mainly sold by Frisch. Dippel also produced Prussian Blue during his stay in the Netherlands until 1714. Diesbach and Frisch tried to protect the secret of Prussian Blue production because of its great commercial success. Once the secret was given away in 1724, production and research started in various European countries. The use of Prussian Blue as a blue pigment still continues today. Although Prussian Blue has been known in the scientific community for 285 years and has attracted much research ever since, new and promising areas of application are still being explored today.

REFERENCES AND NOTES

- The Royal Prussian Society of Sciences was founded in 1700 in Berlin under the name Electoral Brandenburg Society of Sciences. Gottfried Wilhelm Leibniz (1646-1716), residing from 1676 in Hannover who initiated the founding of this society, was appointed president, a post he held until his death. One year after the founding of the Society Elector Friedrich III. of Brandenburg crowned himself in Königsberg (the modern Kaliningrad in Russia) the first king in Prussia (Friedrich I.), starting the short history of the Kingdom of Prussia (1701-1918). Therefore, the name of the Society of Sciences changed to Royal Prussian Society of Sciences. In 1744 it was renamed the Royal Academy of Sciences.
- (J. L. Frisch ?), "Notitia Caerulei Berolinensis Nuper Inventi," *Miscellanea Berolinensia ad incrementum Scientiarum*, **1710**, *1*, 377-378.
- Anon., "Nachricht von dem vor kurzem erfundenen Berlinerblau," *Physicalische und Medicinische Abhandlungen der Koeniglichen Academie der Wissenschaften zu Berlin*, **1781**, *1*, 95-97.
- Stahl, a physician and chemist, was professor of medicine at the university in Halle from 1694 to 1715. Then he moved to Berlin to become appointed physician to King Friedrich Wilhelm I, the son of King Friedrich I. Stahl died in Berlin.
- G. E. Stahl, *Experimenta, Observationes, Animadversiones, CCC Numero Chymicae et Physicae*, Ambrosius Haude, Berlin, 1731, 280-283.
- Many of Leibniz' letters and those sent to him are preserved (about 15,000 letters to and from about 1,100 correspondents) and part of these preserved letters were already been published in the 19th century. Others are still waiting to be published. Since 2007, the correspondence of Leibniz is registered in the UNESCO world documentary heritage Memory of the World. In 1901, work was started on publishing a complete critical edition of Leibniz's writings and correspondence. Since then the Academy Edition ("Akademie-Ausgabe") has been publishing the different series of Leibniz's writings and correspondence, a task that will continue for an estimated 30 years to come. This Academy edition is being prepared today by four research centers (in Hannover, Münster, Potsdam, and Berlin) of two local German science academies (Göttingen Academy of Sciences and Berlin-Brandenburg Academy of Sciences).
- Hannover was the residence of the Duke of Braunschweig-Lüneburg. Leibniz worked as Privy Counselor of Justice for the Duke.
- L. H. Fischer, Ed., *Joh. Leonh. Frisch's Briefwechsel mit G. W. Leibniz*, Georg Olms Verlag, Hildesheim, New York, 1976 (reprint of the book from 1896).
- The town of Wolfenbüttel was the residence of Anton Ulrich Duke of Braunschweig-Wolfenbüttel. Part of his time Leibniz worked for him as a librarian.
- At this time, for preparing the very expensive natural pigment ultramarine ($\text{Na}_{8-10}\text{Al}_6\text{Si}_6\text{O}_{24}\text{S}_{2-4}$), the mineral lapis lazuli was imported to Europe from Asia by sea (ultramarine literally means 'beyond the sea') and further ground and processed in local factories. A process for the production of synthetic ultramarine was discovered in 1826.
- His father was Joseph Werner (1636-1710), first director of the Academy of Arts in Berlin from 1696, who returned to Switzerland in 1706.
- J. Bartoll, B. Jackisch, M. Most, E. Wenders de Calisse, and C. M. Vogtherr, "Early prussian blue: blue and green pigments in the paintings by Watteau, Lancret and Pater in the collection of Frederick II of Prussia," *Technè*, **2007**, *25*, 39-46.
- C. I. Gerhardt, Ed., *Leibnizens mathematische Schriften*, Part 1, Ch. 3, "Briefwechsel zwischen Leibniz, Jacob Bernoulli, Johann Bernoulli und Nicolaus Bernoulli," Verlag H. W. Schmidt, Halle, 1855, 858-878.
- G. W. Leibniz, *Sämtliche Schriften und Briefe*, Reihe I, Allgemeiner, politischer und historischer Briefwechsel, Transkriptionen November 1703-November 1716, n° 391, 471-472. (version from 14.8.2007)
- Wilhelm (Guillaume) Homberg (1652-1715) was a German scientist born in Batavia (the modern Jakarta in Indonesia) and living in France from 1682.
- J. C. Adelung, "Johann Conrad Dippel, ein indifferentistischer Schwärmer," in *Geschichte der menschlichen Narrheit*, Part 1, Weygand, Leipzig, 1785, 314-347.
- K. Buchner, "Johann Konrad Dippel," in Friedrich von Raumer, Ed., *Historisches Taschenbuch*, 3. Folge, 9. Jahrgang, F.A. Brockhaus, Leipzig, 1858, 207-355.
- E. E. Aynsley and W. A. Campbell, "Johann Konrad Dippel, 1673-1734," *Med. Hist.*, **1962**, *6*, 281-286.
- Dippel was born at Frankenstein castle near Darmstadt in Hesse (Germany) in 1673. His family lived in a nearby village and fled during a French raid in the Franco-Dutch War (1672-1678) to the castle Frankenstein. He studied theology in Giessen (Hesse, Germany) from 1689 to 1693 and in Strasbourg (Alsace, France) from 1695-1696. In Strasbourg he became a radical pietist. Pietism was a movement within Lutheranism at that time. From Strasbourg he moved back to Hesse in 1696.
- This is now Kostrzyn in Poland, a town with a big Prussian fortress and prison at that time.
- He had to leave the Netherlands again, because of a theological book which contained religious opinions that were not tolerable even in the Netherlands. Dippel next moved to Altona, at that time a Danish town. Today it is part of Hamburg, Germany. From 1719 until 1726 he was imprisoned on the Danish island of Bornholm. In 1726 he moved to Sweden but was forced to leave in 1728. He spent the last years of his life near castle Berleburg by Casimir von Wittgenstein, not far from the border to his home country Hesse.
- J. E. Berger, *Kernn aller Fridrichs-Städtischen Begebenheiten*, manuscript Berlin State Library - Prussian Cultural Heritage, Ms. Bor. Quart. 124, Berlin, ca 1730, 26.

23. J. Woodward, "Praeparatio Caerulei Prussiæ ex Germania missa ad Johannem Woodward," *Philos. Trans. R. Soc.*, **1724**, 33, 15-17.
24. J. Brown, "Observations and experiments upon the foregoing preparation," *Philos. Trans. R. Soc.*, **1724**, 33, 17-24.
25. John Woodward was appointed professor of medicine in Gresham College in London.
26. Etienne-Francois Geoffroy was a French physician and chemist best known for his affinity tables.
27. Anon., "Sur le Bleu de Prusse," *Hist. Acad. R. Sci.*, **1725**, 33-38.
28. É.-F. Geoffroy, "Observations sur la Preparation de Bleu de Prusse ou Bleu de Berlin," *Mém. Acad. R. Sci.*, **1725**, 153-172.
29. E.-F. Geoffroy, "Nouvelle Observations sur la Preparation de Bleu de Prusse," *Mém. Acad. R. Sci.*, **1725**, 220-237.
30. C. Asai, "'Handmade' Berlinerblau," *ZKK Zeitschrift für Kunsttechnologie und Konservierung*, **2004**, 18, 268-292.
31. Pierre Joseph Macquer, a French chemist, was the author of the first chemical dictionary (1766).
32. P. J. Macquer, "Mémoire sur une nouvelle espèce de teinture bleue, dans laquelle il n'entre ni pastel ni indigo," *Mém. Acad. R. Sci.*, **1749**, 255-264.
33. L. J. M. Coleby, "A History of Prussian Blue," *Ann. Sci.*, **1939**, 4, 206-211.
34. C. W. Scheele, "Über die färbende Materie in Berlinerblau," *Neue Schwed. Akadem. Abhandl.*, **1782**, 3, 256-266.
35. J. L. Gay-Lussac, "Recherches sur l'acide prussique," *Ann. Chim.*, **1815**, 95, 136-231.
36. J. F. Keggin and F. D. Miles, "Structures and Formulae of the Prussian Blues and Related Compounds," *Nature*, **1936**, 137, 577-578.
37. H. J. Buser, D. Schwarzenbach, W. Petter and A. Ludi, "The Crystal Structure of Prussian Blue: $\text{Fe}_4[\text{Fe}(\text{CN})_6]_3 \cdot x\text{H}_2\text{O}$," *Inorg. Chem.*, **1977**, 16, 2704-2710.
38. M. Ware, *Cyanotype: The History, Science and Art of Photographic Printing in Prussian Blue*, National Museum of Photography, Film and Television, Bradford, UK, 1999.
39. D. F. Thompson and E. D. Callen, "Soluble or Insoluble Prussian Blue for Radiocesium and Thallium Poisoning?" *Ann. Pharmacother.*, **2004**, 38, 1509-1514.
40. V. D. Neff, "Electrochemical Oxidation and Reduction of Thin Films of Prussian Blue," *J. Electrochem. Soc.*, **1978**, 125, 886-887.
41. A. Kraft, M. Rottmann and K.-H. Heckner, "Large-area Electrochromic Glazing with Ion-conducting PVB Interlayer and two Complementary Electrodeposited Electrochromic Layers," *Sol. Energy Mater. Sol. Cells*, **2006**, 90, 469-476.
42. K. Itaya, N. Shoji, and I. Uchida, "Catalysis of the Reduction of Molecular Oxygen to Water at Prussian Blue Modified Electrodes," *J. Am. Chem. Soc.*, **1984**, 106, 3423-3429.
43. F. Ricci and G. Paleschi, "Sensor and Biosensor Preparation, Optimisation and Applications of Prussian Blue Modified Electrodes," *Biosens. Bioelectron.*, **2005**, 21, 389-407.
44. M. Jayalakshmi and F. Scholz, "Charge-discharge Characteristics of a Solid State Prussian Blue Secondary Cell," *J. Power Sources*, **2000**, 87, 212-217.
45. G. Selvarani, S. K. Prashant, A. K. Sahu, P. Sridhar, S. Pitchumani, and A. K. Shukla, "A Direct Borohydride Fuel Cell Employing Prussian Blue as Mediated Electron-transfer Hydrogen Peroxide Reduction Catalyst," *J. Power Sources*, **2008**, 178, 86-91.

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THE HISTORY OF OZONE. VI. OZONE ON SILICA GEL (“DRY OZONE”) (1)

Mordecai B. Rubin, Technion-Israel Institute of Technology

Introduction

As part of a general study of the interaction between gases and solids in the laboratory of Alfred Magnus (Fig. 1) at the University of Frankfurt, Magnus and Grähling (2) reported the adsorption of ozone on silica gel in 1929. These measurements were complicated by the thermal instability of ozone, which, as shown by Magnus and Grähling, was further catalyzed by silica gel. A second problem was the low concentration of ozone in oxygen obtained from conventional ozone generators. Nonetheless, Magnus and Grähling found that considerable amounts of ozone could be adsorbed on silica gel at low temperatures where decomposition was not a problem. The average heat of adsorption of ozone, measured by taking the difference between pure oxygen and ozone-oxygen mixtures was 5,600 cal/mole with a temperature coefficient of -175 cal/deg. The corresponding values for oxygen were 3,200 cal/mole and -30 cal/deg. Thirty years later Cook et al (3) performed a similar study with results in agreement with those of the earlier work. They measured the adsorption isotherms (Fig. 2) for ozone on silica gel over the range -78.5° C to -140° C as a function of ozone

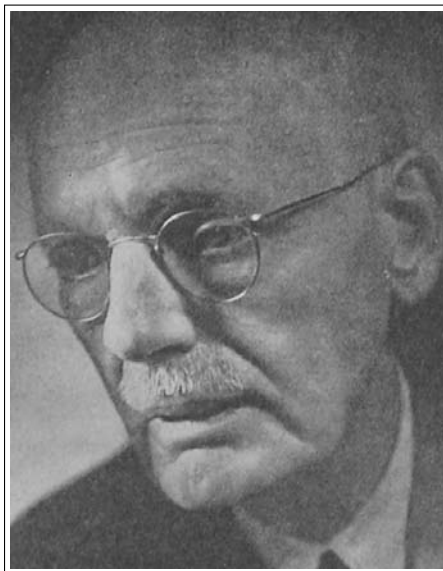


Figure 1. Alfred Magnus, Un. of Frankfurt, 1880-1960.

partial pressure. As can be seen in Figure 2, adsorption increased markedly with decreasing temperature, the significance of temperatures below the boiling point of ozone (-112° C) is not clear. The measurements were made by passing ozone-enriched oxygen (ca 2% ozone) from a silent discharge apparatus through a tube packed with silica gel until compositions of the entrance and exit gases were identical. The ozone was then desorbed and analyzed iodimetrically.

More recently Atyaksheva and co-workers (4) have studied the adsorption of ozone on silica gel in considerable detail. Bulanin et al. (5) reported that the IR spectrum of different isotopic ozone species on silica gel at 80 K exhibited hydrogen bonding of terminal oxygen atoms with silanol groups but that only minor changes from the spectrum of pure liquid ozone were observed. The only report on the long-term stability of ozone on silica gel is due to Hesse and Bayer (6) who claimed that 91% of adsorbed ozone was retained after 2 weeks storage at -75° C (but see below).

Silica gel is well-known to have a high affinity for water; commercially supplied silica gels used in most of the work described here generally contained about 3% water. This can be reduced by heating under vacuum.

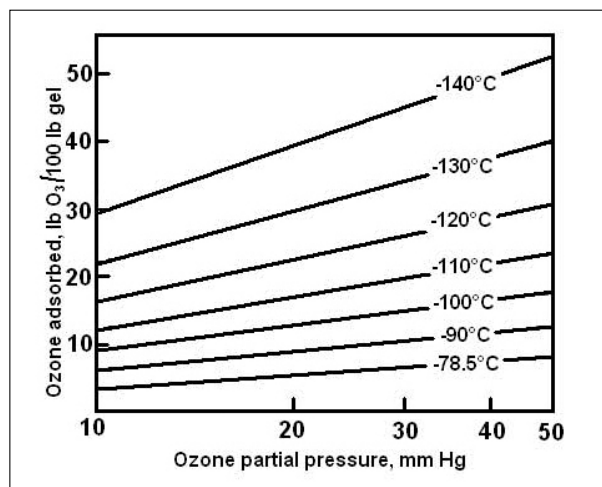


Figure 2. Adsorption isotherms for ozone on Davison silica gel at -78.5°C to -140°C and total pressure of 1 atm. Reprinted with permission from Ref. 3. Copyright 1959 American Chemical Society.

Cook et al reported that the adsorption capacity of silica gel which was repeatedly recycled with ozone enriched oxygen was reduced markedly but could be regenerated by heating in vacuo; they attributed this to accumulation of water on the silica gel. Ishii et al (7) claimed that concentrations of 1-2% water on silica gel decreased the rate of decomposition at -80°C significantly. The function of adsorbed water as a reagent for ozonide decomposition will be mentioned in the section on organic reactions.

Desorption

A number of simple procedures are available for desorbing ozone from silica gel. These include passing a gas (not necessarily oxygen) through the silica gel, warming above the temperature at which adsorption occurred (microwave heating has also been used (8)), reduction in pressure, or a combination of these. Thus there is considerable flexibility in the desorption process. While Hesse and Bayer (6) reported in 1964 that 95% of the adsorbed ozone could be recovered by desorbing with a stream of nitrogen gas, it is not clear if the 5% loss is characteristic of desorption or was due to losses in the manipulations required for analysis. We note that a similar loss was observed by Riesenfeld and Schwab (9) in analyses of highly purified ozone. Edgar and Paneth (10) made a careful study and concluded that there was complete recovery of ozone adsorbed at liquid oxygen temperature; desorption was effected by warming to -120°C in a stream of oxygen. Other workers seem to have assumed, without experimental verification, that desorption is quantitative.

Although desorbed ozone seems to be perfectly normal in its chemistry, it has variously been reported to contain singlet oxygen (11) or to consist of clusters of ozone (12, 13). The latter workers also reported theoretical calculations in support of the existence of O_6 and O_9 . These reports have not elicited any response.

Storage of Ozone

Examination of Fig. 1 shows that even the few percent of ozone in oxygen provided by conventional ozone generators, when adsorbed at the convenient temperature of approximately -78°C (14), will achieve a loading of 5-10% by weight of ozone on silica gel; this ozone is quite stable if maintained at low temperature. Bailey and Reader (15) estimated that the ratio of ozone to oxygen is on the order of 8,000:1 while Cook et al (3) stated that "very little" oxygen was adsorbed. Furthermore, convenient procedures are available for desorbing the ozone when desired. These facts combined to provide an attractive possibility for storing ozone on silica gel for use when desired, provided that this can be done safely. The Linde company, worldwide purveyors of gases, made a significant investment in this possibility.

The first report in the direction of safe storage was due to Cook et al (16) at Linde in 1956 who tested the explosion hazard of silica gels containing adsorbed ozone by igniting an electric spark within or above the solid material; they reported that loadings of up to 10% of ozone did not present an explosion hazard. They went on (3) in 1959 to describe a pilot plant for storage of ozone. This consisted of three 6" diameter aluminum tubes each filled with 125 lbs of Davison silica gel to a height of 15 feet. Cooled ozone in oxygen, as produced by a Welsbach generator (2% ozone), was passed through the cooled columns until saturation. Oxygen was recycled in the closed system and the ozone was desorbed by evacuation. An alternative method for desorbing ozone, warming, was not practical with large columns. After 200 hours operation, the capacity of the silica gel was reduced by 50%, presumably because of adsorption of water vapor as noted above. The authors concluded that the method described provides a reasonable procedure for storing ozone for use on demand. A 1975 Japanese patent (17) makes pikers out of Cook et al. It describes a system operating at -80°C containing tons of silica gel with the corresponding 10% of ozone. Desorption was effected by nitrogen gas and the operational parameters were adjusted so that the ozone concentration in the effluent gas mixture remained nearly constant.

One application of such storage is for so called "load leveling" (18, 19). The ozone production unit in, for example, a water purification plant, need not be designed to meet peak demand but only to produce the average amount of ozone required. When demand is low, the excess production can be stored to be available when required.

Cook et al (3) also suggested that it might be possible to provide adsorbed ozone in cylinders in the same manner used for supply of other gases. However, as they pointed out, it would be necessary to keep such cylinders at low temperature and provide special safety features in the event of failure of the cooling system. To the best of our knowledge, this has not proved to be a practical procedure although a Japanese patent (20), without safety features, exists.

A method for water purification described by Tizaoui and Slater (21) involved contacting a bed of ozone adsorbed on silica gel with the water to be purified; the silica gel was regenerated by heating after use. An ingenious application for liquid purification was described by Leitzke (22) in which desorption of ozone from silica gel was achieved by the vacuum from an injection pump using the liquid to be purified (drinking water, waste water e.g.) so that the desorbed ozone was introduced directly into the liquid.

In addition to the use for water purification mentioned above, a number of other applications of ozone on silica gel have been described. These include (1) analysis of atmospheric ozone, (2) changing the composition of the ozone stream, and (3) use in organic chemistry.

(1) Analysis of Atmospheric Ozone

Concentrations of ozone found in the atmosphere often lie at or below the limit of sensitivity of the conventional iodimetric determination; this method also suffers from a lack of specificity for ozone. These problems were overcome using adsorption of ozone on silica gel by Paneth and Edgar (23) and by Briner (24) independently in 1938, nine years after Magnus and Grähling's original report. Paneth and Edgar accumulated the ozone from 1,000-1,500 liters of air by adsorption on specially prepared silica gel at liquid oxygen temperature (-183°C), thus multiplying the amount of ozone manyfold. Desorption was achieved by warming to -120°C in a stream of oxygen. Control experiments showed (10) that complete recovery of ozone was achieved under these conditions. The desorbed gas was shown to be ozone by

use of tetrabase paper and by spectroscopy, and subjected to iodimetric analysis. Adsorbed nitrogen dioxide was not affected but could be desorbed at higher temperature (they used boiling water) and analyzed. After a very detailed preliminary study (10) Edgar and Paneth (25) found that the ozone concentration in London air was in the range 0.4-4.5 ppm and the nitrogen dioxide concentration in the range 0.05-2.0 ppm. This procedure for ozone analysis was also used by Jacobi (26) who passed 2000 l of air over silica gel at liquid oxygen temperature and by Sadikov (27) who found a value of 0.8×10^{-8} g/l for the ozone concentration in his sample of air.

In the early days of smog studies in Los Angeles, Littman and Marynowski (28) were able to show that ozone is the principal oxidant in the Los Angeles atmosphere; they flushed the adsorbed gases from a large sample of air into an optical cell and identified ozone spectroscopically.

(2) Changing Composition of the Ozone Stream

When ozone generated from pure oxygen is adsorbed on silica gel, ozone of high purity is retained on the silica gel. This is probably the simplest way to obtain pure ozone since the low temperature condensation procedure commonly used invariably gives an ozone-oxygen mixture which requires further manipulation to obtain oxygen-free ozone. The first application of this fact was due to Bailey and co-workers (15, 29) in 1961 who required oxygen-free ozone in order to establish if oxygen was formed in the course of an ozonolysis reaction. They performed the desorption using nitrogen gas to obtain a stream of ozone in nitrogen; a conventional oxygen analyzer was then used to determine if oxygen had been formed in the ozonolysis. Hesse and Bayer reported (6) that they used such a procedure routinely in ozonolysis of organic compounds; problems arising from the presence of oxygen during the ozonolysis were avoided. Appropriate adjustments of temperature and gas flow allow good control over the composition of the ozone stream giving considerable flexibility in experimental procedures.

It is also possible, using warming or reduced pressure, to desorb ozone and obtain a stream of pure ozone of desired pressure. This procedure has been used by, among others, Coleman et al (30) for growing films of $\text{Ba}_2\text{YCu}_3\text{O}_7$ and by Sukuzaki et al (31) for treating stainless steel fiber.

(3) Organic Chemistry (“Dry Ozone”)

The application of ozone on silica gel to organic compounds was developed by Yehuda Mazur (Fig. 3) and coworkers (32) at the Weizmann Institute of Science who published about 20 papers on the subject over a ten year period beginning in 1975. They coined the term Dry Ozone for these reactions to emphasize the fact that ozonolyses of organic compounds were performed on silica gel in the absence of any solvent. This procedure avoids possible complications from solvent and excess oxygen. Two additional factors involved are the reduced mobility of reaction intermediates and the possibility of conformational restrictions due to interactions with silica gel.

Shortly after the Mazur papers began to appear, a number of reports, mainly concerned with regioselectivity of hydroxylation reactions were published by A. L. J. Beckwith (Fig. 4) and co-workers (33) at the University of Adelaide and ingenious applications of Dry Ozone to compounds containing a cyclopropane ring and a variety of polycyclic compounds appeared from the laboratory of A. de Meijere (Fig. 5) et al at the University of Göttingen.

The simple general procedure used is illustrated by the 1986 Organic Syntheses (34) preparation of 1-adamantanol (**2**) from adamantane (**1**) in nearly 90% yield. This reaction is a general one; hydrotrioxides (ROOOH) have been shown to be intermediates (35, 36). The substrate is adsorbed on silica gel by rotary evaporation at reduced pressure of a mixture of silica gel and a solution of substrate in a volatile solvent, cooled in a Dry Ice-2-propanol bath (14), and ozone-enriched oxygen flowed through the vessel at this temperature until the deep blue color of ozone develops. Free warming to room temp. is followed by elution of product(s) with the appropriate solvent. Minor products in the reaction of **1** (<7%) were 2-adamantanone

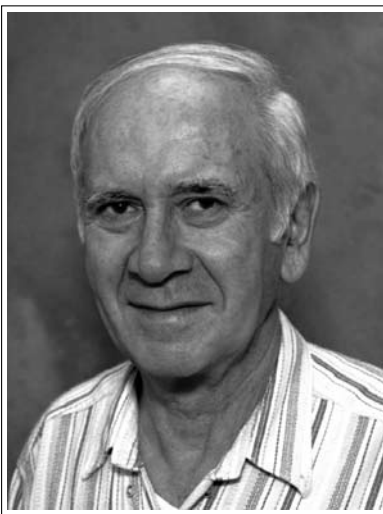


Figure 3. Yehuda Mazur, Weizmann Institute of Science, 1925-2004

and adamantan-1,3-diol. We note that an important variable in these reactions seems to be the presence of water which normally constitutes a few percent of commercial silica gels; this may be reduced to a much lower value by heating in vacuo.

The reactions of organic compounds with Dry Ozone were reviewed briefly in 1979 by de Meijere (37) and extensively in 1983 by Mazur's co-workers, Keinan and Varkony (38). We will not attempt to repeat these reviews but rather present a few examples illustrating the novelty and utility of this relatively simple modification of the conventional ozonolysis procedure.

The selective oxidation at tertiary positions illustrated by the adamantane reaction was a general phenomenon and occurred with retention of configuration. The exceptions were substances having a methylene group adjacent to a cyclopropyl ring, as illustrated for the reaction of ethylcyclopropane (**3**) with Dry Ozone. The single product (95% yield) was methyl cyclopropyl ketone (**4**). De Meijere and Proksch, who reported this result (39), applied it to a variety of substances containing a 3-membered ring including the conversion (40) of hydrocarbon **5** to diketone **6**. This was subsequently transformed in 16% overall yield to the 6-rotane **7**. The de Meijere group investigated the reactions of a variety of polycyclic systems with Dry Ozone including studies of regio- and stereoselectivity and succeeded (41) in the first synthesis of a “hyperstable” bridgehead olefin.

The restricted mobility enforced by the adsorbent is nicely illustrated by the results of Den Besten and Kinstle (42) in the ozonolysis of pentene (**8**). In pentane solution this reaction affords a mixture (80% overall yield) of three ozonides representing all possible combinations of the intermediates, acetaldehyde and propionaldehyde with zwitterions **10** and **11**. In contrast, Den Besten and Kinstle, using Dry Ozonation with silica gel dried at 300° C under vacuum, obtained over 90% yield of the single ozonide **9**. Presumably the carbonyl and zwitterionic fragments produced



Figure 4. Athelstan Lawrence Johnson Beckwith, Australian National University, b. 1930.

were sufficiently restrained by the medium to combine before separating as they do in solution. In this and in alkene reactions in general with Dry Ozone the peroxidic products observed in solution reactions are generally not formed.

In many cases, final products of ozonide decomposition, aldehydes, ketones, and or carboxylic acids were observed in alkene reactions (42, 43) with ozone on silica gel. This is presumably effected by water present in the silica gel reacting with the ozonide. Decomposition with water was the earliest method used for obtaining the stable, final reaction products in many ozonolysis reactions.

Finally, Keinan and Mazur (44) studied the oxidation of amines to nitro compounds in considerable detail. This conversion was exploited by Giuliano and Diesenroth (45) in a key step of a synthesis of **13** where the amino group in **12** was converted to a nitro group in 80% yield.

In the nearly 25 years following the 1983 review (38) on Dry Ozone, only a few papers have appeared on the subject. Mazur became absorbed in the reactions of atomic oxygen with organic compounds, Beckwith became very much involved in free radical chemistry, and de Meijere turned to new cyclic systems and other aspects of his multi-faceted research program. The few papers which did appear included work on a synthesis in the sugar series (46), reaction of phenanthrene (47), of 2,3-di-*t*-butylbutadiene and monoterpenes (48, 49), of aromatic compounds (50), and the adamantane reaction (51-53). We have found no references to organic reactions involving ozone on silica gel after 1997. For the period 1980-2007, SciFinder affords a total of over 10,000 references to ozonolysis but only 52 to the combined terms ozonolysis silica gel. In view of the simplicity of the procedure and the clean reactions observed in many cases, it is puzzling to find that the application of Dry Ozone to organic compounds appears to have disappeared from the current chemical literature.

Replacement of silica gel by polyethylene (48, 49) favors isolation of ozonides, perhaps because of the minimal amount of water present. Ozone is also adsorbed on high silica zeolites (54). While fundamental studies have not been reported, a variety of applications have



Figure 5. Armin de Meijere, University of Göttingen, b. 1939.

been described, most of them appearing in the patent literature, including destruction of ozone, application to purification of water, and preparation of high concentration ozone

Summary

Considerable amounts of ozone can be adsorbed on silica gel at low temperature. Loadings of up to 10% ozone do not represent an explosion hazard if maintained at these temperatures and are stable for extended periods of time. Desorption of ozone can be effected by flowing a gas through the silica gel, by raising the temperature, or by reducing the pressure. Applications of adsorbed ozone include storage of ozone, water treatment, analysis of very low concentrations of ozone found in the atmosphere, changing the composition of the ozone stream, and eliminating some of the complications observed in organic reactions. Adsorption of ozone on silica gel provides a simple means for obtaining high purity ozone. Adsorption of ozone on polyethylene and on high silica zeolites has also been reported.

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REFERENCES AND NOTES

1. For the preceding paper in this series see M. B. Rubin, "The History of Ozone. V," *Bull. Hist. Chem.*, **2007**, *32*, 45-56.
2. A. Magnus and K. Grähling, "Über die Adsorption von Sauerstoff und Ozon an Kieselsäuregel," *Z. Phys. Chem. Abt. A*, **1929**, *145*, 27-47. Alfred Magnus, 1880 (Alex-

- andria, Egypt)-1960. Studied in Munich 1898-1905, D. phil. Munich 1905; 1905-1908 in Berlin. From 1910 Dozent, physical chemistry, Tübingen, 1922-46 Assoc. Prof., Frankfurt, 1946 Prof. and Director Physical Chemistry Institute, Emeritus 1949. Concealed by Bonhoefer in Leipzig during the later Nazi years. Hartmann (*Pure Appl. Chem.*, **1977**, *49*, 827-837) credits him with founding the electrostatic theory of complex compounds which provided a basis for ligand-field theory. He was also active in thermochemical measurements and in the theoretical and experimental aspects of the interaction between gases and solids.
3. G. A. Cook, A. D. Kiffer, C. V. Klumpp, A. H. Malik, and L. A. Spence, "Separation of Ozone from Oxygen by a Sorption Process," in *Ozone Chemistry and Technology, Adv. in Chem. Series, No. 21*, Am. Chem. Soc., Washington, DC, **1959**, 44-52. Gerhard A. Cook, 1907-1993. B. Sc. (1928), M. Sc. (1933), Ph. D., (1935) Un. of Michigan. Instructor, Case Inst. of Tech., 1935-37. Research chemist, Linde Div., Union Carbide Corp., 1937-57, Asst. Manager research 1957-67. Consultant, Nat. Un. Asuncion, Paraguay 1967-69. Adjunct Prof. and Exec. Director, Chem. Dept., State Un. of New York at Buffalo 1967-1974.
 4. L. F. Atyaksheva and G. I. Emel'yanova, "Physical-chemical processes in the sorption of dilute ozone and oxygen.," *Zh. Fiz. Khim.*, **1990**, *64*, 1741-9 and papers cited therein.
 5. K. M. Bulanin, A. V. Alexeev, D. S. Bystrov, J. C. Lavalley, and A. A. Tsyganenko, "IR Study of Ozone Adsorption on SiO₂," *J. Phys. Chem.*, **1994**, *98*, 5100-5103.
 6. G. Hesse and E. Bayer, "Ozonspaltung organischer Verbindungen in Abwesenheit von Sauerstoff," *Z. Naturforsch.*, **1964**, *19b*, 875-7. Gerhard Hesse, born 1908. Studied Bonn and Munich. Habilitation Munich 1937. Privat Dozent Marburg 1938, Assoc. Prof. Freiburg 1944. 1952-76 Prof and Dir. Inst. Org. Chem. Un. Erlangen-Nürnberg. Member Bavarian Acad. Sci, Fresenius prize of German Chem. Soc. 1972. Best known for coupling of prep. org. chem. with analytical methods, esp. chromatography.
 7. J. Ishii, A. Wakaizumi, T. Hirano, and Y. Satomi, "Concentrating or Storing of Ozone," *JP 50126591 1975 Japan Oxygen Co., Ltd., Japan CAN 85:65339, 1975*.
 8. J. Mizutani, "Apparatus for Producing High-concentration Ozonized Water," *JP 2001259391 CAN 135:261941, 2001*.
 9. M. B. Rubin, "The History of Ozone. IV. The Isolation of Pure Ozone and Determination of its Physical Properties," *Bull. Hist. Chem.*, **2004**, *29*, 99-106, Ref. 24.
 10. J. F. Edgar and F. A. Paneth, "Separation of Ozone from other Gases," *J. Chem. Soc.*, **1941**, 511-19. Friedrich Adolf Paneth, 1887-1958. Studied Munich and Vienna, D. phil. 1910, Vienna. 1913, Glasgow Un.. Habilitation 1913. 1919, Assoc. Prof. Un. of Hamburg, 1922, 1926. Assoc. Prof., Un. of Berlin, 1926-7 Baker lecturer, Cornell Un.. 1929, 1929-33 Prof and Dir. Chem. Inst. Un. Königsberg. 1933 guest Imperial College, exiled from Germany. London, 1938 Reader in Atomic Chem. U of London, 1939-53 Prof., 1947-53 Dir. Londonderry Lab. Radiochem., Un. of Durham, since 1953 Dir. MPI, Mainz. 1916 Lieben Prize (Austrian Acad. of Sci.), 1952 Lavoisier medal, 1953, Stas medal, 1956 Liebig medal.
 11. A. I. Voloshin, G. L. Sharipov, V. P. Kazakov, and G. A. Tolstikov, "Generation of Singlet Oxygen on Adsorption and Decomposition of Ozone on Silica Gel," *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1986**, 2613-15.
 12. A. Murai, T. Nakajima, and N. Tahara, "Estimation of ozone-cluster using MOPAC program," *J. Comput. Chem. Jpn.*, **2002**, *1*, 123-128.
 13. A. Murai and T. Nakajima, N. Tahara, "Verification of Ozone Clusters (O₆ and O₉)," *Ozone: Science & Engineering*, **2003**, *25*, 211-221.
 14. H. J. E. Loewenthal, "Minus 78 degrees," *Chem. Br.*, **1983**, *21*, 917. Loewenthal has pointed out that immersion of a container in a dry-ice bath does not guarantee that the temperature of the contents will be -78° C, even without taking into account the occurrence of exothermic processes. This will be particularly true if the contents are an unmixed solid material such as silica gel.
 15. P. S. Bailey and A. M. Reader, "The Use of an Oxygen Analyser in Ozonisation Mechanism Studies," *Chem. Ind. (London)*, **1961**, 1063-64, Philip Sigmon Bailey, 1916-1998. B.S. 1937 Oklahoma Baptist Un., M. S. 1940 Un. Oklahoma, Ph.D. 1944, Un. Virginia. Un. Texas, Austin, Asst. Prof. 1945, Assoc. Prof. 1949, Prof. 1957, emeritus 1984. Fulbright Grant, Un. Karlsruhe 1953-4. An outstanding figure in ozone chemistry, he authored the definitive two-volume monograph on this subject.
 16. G. A. Cook, E. Spadinger, A. D. Kiffer, and C. V. Klumpp, "Explosion Limits of Ozone-oxygen Mixtures," *J. Ind. Eng. Chem.*, **1956**, *48*, 736-41.
 17. H. Okada and U. Maeda, "Continuous Manufacture of Ozone-nitrogen Mixtures of Constant Ozone Concentration.," *JP50116390 CAN 84:124031, 1975*.
 18. A. Murai, N. Tahara, and T. Nakajima, "Ozone Storage Oriented to Power Load Leveling," *Ozone: Science & Engineering*, **2002**, *23*, 171-180.
 19. Y. Sakata, "The Economical Ozone Disinfection System by using Ozone Adsorbing Technology," *Kankyo Eisei Kagaku Kenkyu*, **2005**, *19*, 129-133. *CAN 143:215886*.
 20. K. Koike and G. Inoue, "Storage Container for Condensed High-concentration Ozone Gas Transportation," *JP11002398 CAN130:83680, 1999*.
 21. C. Tizaoui and M. J. Slater, "The Design of an Industrial Waste-water Treatment Process using Adsorbed Ozone on Silica Gel," *Process Safety and Environmental Protection*, **2003**, *81*, 107-113.
 22. O. Leitzke, "Improvement in the Generation and Feeding of Ozone by a New Adsorption-desorption Process," *Chem. Ing. Technik*, **1984**, *56*, 473-6.
 23. F. A. Paneth and J. L. Edgar, "Concentration and Measurement of Atmospheric Ozone," *Nature*, **1938**, *142*, 112-13.

24. E. Briner, "Adsorption et dosage de l'ozone de l'air au moyen du gel de silice refroidi," *Helv. Chim. Acta.*, **1938**, *21*, 1218-1221. Emile Briner, 1879-1965. Born near Geneva and spent his entire professional life at Un. Geneva. Doctor's degree with Guye, Privatdozent 1903, Assoc. Prof. and Prof of special technical chemistry 1918, Prof. 1922, retired 1954. Published about 150 papers on ozone, including 70 on ozonolysis; but his contributions were eclipsed by the general adoption of the Criegee mechanism in the 1950s. Honorary doctorate, Un. Paris 1949, very active in Swiss chemical societies.
25. J. L. Edgar and F. A. Paneth, "The Determination of Ozone and Nitrogen Dioxide in the Atmosphere," *J. Chem. Soc.*, **1941**, 519-27.
26. R. B. Jacobi, "The Micromasurement of Radioelements and Rare Gases," *Sci. J. Roy. Coll. Sci.*, **1939**, *9*, 16-23.
27. V. Sadikov, "Determination of Ozone in Air," *Priroda*, **1939**, 64-5.
28. F. E. Littman and C. W. Marynowski, "Identification of Ozone in the Los Angeles Atmosphere," *Anal. Chem.*, **1956**, *28*, 819-25. Fred Emanuel Littman, 1917-2004.
29. A. H. Riebel, R. E. Erickson, C. J. Absire, and P. S. Bailey, "Ozonation of Carbon-Nitrogen Double Bonds. I. Nucleophilic Attack of Ozone," *J. Am. Chem. Soc.*, **1960**, *82*, 1801-07.
30. E. Coleman, T. Siegrist, D. A. Mixon, P. L. Trevor, and D. J. Trevor, "A Versatile Low-pressure Ozone Source," *J. Vac. Sci. Tech. A: Vacuum, Surfaces, and Films*, **1991**, *9*, 2408-9.
31. S. Sukuzaki, K. Koike, K. Takahashi, and S. Yamada, "Surface Modification and Regeneration of Nonwoven Fabric of Stainless Steel Fiber by Highly-concentrated Gaseous Ozone," *Hyomen Gijutsu*, **2006**, *57*, 440-444.
32. Z. Cohen, E. Keinan, Y. Mazur, and T. H. Varkony, "Dry Ozonation. Method for Stereoselective Hydroxylation of Saturated Compounds on Silica Gel," *J. Org. Chem.*, **1975**, *40*, 2141-2142. Yehuda Mazur, 1925-2004. Born Poland, immigrated to Israel in 1939. M.Sc. Jerusalem 1947, Ph. D. (Ruzicka) ETH Zürich 1952. Joined Weizmann Institute of Science in 1954, Senior Scientist 1959, Assoc. Prof. 1963, Prof. 1976, Head of Dept. Org. Chem. 1979-90. Visiting Fellow MIT 1959-60, Cambridge Un. 1965, ETH Zürich 1966, Un. Paris-Sud 1984, ANU Canberra 1986. His research interests included thermal and photochemical reactions of steroids, studies of stretched films, the ozone work described herein, and extensive studies of the reactions of atomic oxygen. Ehud Keinan, born 1947. B.Sc. Tel Aviv Un. 1970; M. Sc. Ben Gurion Un., Ph.D. Weizmann Inst. of Science (Y. Mazur) 1977; Postdoctoral fellow Un. Wisconsin (Trost) 1977-80. Weizmann Inst. 1980-87; Technion 1987- , Chem. Dept. Chairman 2004-6. From 1991 simultaneously Adjunct Prof. Dept of Molecular Biology and Skaggs Institute of Chemical Biology, Scripps Res. Inst.
33. A. L. J. Beckwith and T. Duong, "Regioselective Oxidation of Adsorbed Alkyl Hydrogen Succinates by Ozone in Freon 11," *J. Chem. Soc., Chem. Commun.*, **1979**, 690-691 and references therein. Athelstan Lawrence Johnson Beckwith, born 1930 Perth, Western Australia. B.Sc. 1952 Un. Western Australia, D. Phil (Waters) 1956 Oxford Un. 1957, Research officer, CSIRO, Melbourne. Lecturer, Un. Adelaide: 1958-1961, Senior Lecturer 1962-1963, Reader Org. Chem. 1964-65. Prof. Org. Chem. and Head of Dept. 1965-81. 1982 Prof. Phys. Org. Chem., Research School of Chemistry, Australian National Un., Dean 1989-91, emeritus 1996. Research in reaction mechanisms and applications to synthesis with major emphasis on free radical chemistry. A key figure in Australian chemistry at the local and federal levels. Federation medal 2001, Officer of the Order of Australia 2004, FRS 1987, Fellow of the Australian Acad. Sci. 1973.
34. Z. Cohen, H. Varkony, E. Keinan, and Y. Mazur, "Tertiary Alcohols from Hydrocarbons by Ozonation on Silica Gel: 1-Adamantanol," *Org. Synth., Coll. Vol. VI*, **1988**, 43-47.
35. M. Zarth and A. De Meijere, "Zum Mechanismus der Ozonolyse von C-H-Bindungen: SiO₂-Lösungsmittelinfluss, H/D-Isotopieeffekt, Zwischenstufen," *Chem. Ber.*, **1985**, *118*, 2429-2449.
36. E. V. Avzyanova, Q. K. Timerghazin, A. F. Khalizov, S. L. Khursan, L. V. Spirikhin, and V. V. Shereshovets, "Formation of Hydrotrioxides during Ozonation of Hydrocarbons on Silica Gel. Decomposition of Hydrotrioxides," *J. Phys. Org. Chem.*, **2000**, *13*, 87-96 and references therein. For a general review of hydrotrioxides see de Meijere and Wolff, "Über Organo-hydrotrioxide verlaufende Ozonolysen von präparativen Interesse," in H. Kropf, Ed., *Houben-Weyl Methoden der Organischen Chemie*, Thieme-Verlag, Stuttgart, Vol. E13, 971-990, 1118-1122
37. A. de Meijere, "Alte Reagenzien mit neuen Anwendungsmöglichkeiten," *Nachrichten Chem., Technik Lab.*, **1979**, *27*, 177-8, 180-2. Armin de Meijere, born 1939. Studied in Freiburg and Göttingen, D. phil. Göttingen (Luetke), 1966. Postdoctoral work at Yale Un. (Wiberg) 1967-69, Habilitation at Göttingen 1971. Prof. Un. Hamburg 1977-1989. From 1989 Prof. Göttingen, emeritus 2006. Visiting Professor at Technion and numerous other institutions, numerous awards including the Adolf von Baeyer Medal of the German Chemical Society. Over 650 publications, mainly in the areas of small ring compounds, highly strained polycyclic compounds and studies of organometallic complexes, including over 150 publications on the development of new transition-metal-catalyzed and -mediated syntheses..
38. E. Keinan and H. T. Varkony in: S. Patai, Ed. *The Chemistry of Functional Groups, Peroxides*, Wiley, London, **1983**, Ch. 19, 649-682.
39. E. Proksch and A. de Meijere, "Oxidation of Cyclopropyl Hydrocarbons with Ozone," *Angew. Chem., Int. Ed. Engl.*, **1976**, *15*, 761-762.
40. E. Proksch and A. de Meijere, "Convenient synthesis of tetraspiro[2.0.2.1.2.0.2.1]tetradecane-7,14-dione and

- hexaspiro[2.0.2.0.2.0.2.0.2.0.2.0.2.0.2.0]octadecane (“[6]-rotane”),” *Tetrahedron Lett.*, **1976**, 4851-4854.
41. H. Kukuk, E. Proksch, and A. de Meijere, “Bicyclo[4.4.2]dodec-1-ene: the First “Hyperstable” Bridge-head Olefin,” *Angew. Chem., Int. Ed. Engl.*, **1982**, *21*, 306.
 42. I. E. Den Besten and T. H. Kinstle, “Low-Temperature Ozonation of Alkenes Adsorbed on Silica Gel,” *J. Am. Chem. Soc.*, **1980**, *102*, 5968-5969. Ivan Eugene Den Besten. Born 1933. A.B. Calvin College, 1957, Ph.D. Northwestern Un. 1961. Bowling Green State Un., Instructor 1961, to full Professor 1970, retired 2001.
 43. C. Aronovitch, D. Tal, and Y. Mazur, “Ozonolysis of Olefins and Acetylenes Adsorbed on Silica Gel,” *Tetrahedron Lett.*, **1982**, *23*, 3623-6.
 44. E. Keinan and Y. Mazur, “Dry Ozonation of Amines. Conversion of Primary Amines to Nitro Compounds,” *J. Org. Chem.*, **1977**, *42*, 844-847.
 45. R. M. Giuliano and T. W. Diesenroth, “Synthesis of Methyl- α -D-Kijanosid,” *J. Carbohydr. Chem.*, **1987**, *6*, 295-299. Robert Michael Giuliano, 1954-. B.S. Penn State Un. 1976, Ph.D. Un. Virginia 1981, postdoc Un. MD 1981-82. Villanova Un. Asst. Prof. 1982-88, Assoc. Prof. 1988-. Vis. Assoc. Prof. Brown Un. 1990-91.
 46. S. W. Remiszewski, R. R. Whittle, and S. M. Weinreb, “Synthesis of 5-Epi-desosamine via a Stereoselective Intramolecular N-sulfinyl Diels-Alder Cycloaddition,” *J. Org. Chem.*, **1984**, *49*, 3243-3244. Steven Martin Weinreb, born Brooklyn, 1949. B.A. Cornell Un. 1963, Ph.D. Un. Rochester 1967, Postdoc Columbia Un. 1966-67 (Stork), 1968-70 MIT (Büchi). Fordham Un., Asst., Assoc. prof. 1970-78. Penn. State Un. 1978, Prof 1980, from 1987 Marker Professor. Head of Dept. 1994-98. Natural products chemistry. Guggenheim fellow, Sloan Fellow.
 47. T. Yoshikawa, D. H. Giamalva, W. Flory, L. P. Ruhr, D. F. Church, and W. A. Pryor, “Toxicity of Polycyclic Aromatic Hydrocarbons. IV. Effects of Diphenaldehyde, a Major Product of Ozonized Phenanthrene, in Rats,” *Biochem. Int.*, **1987**, *15*, 139-146.
 48. K. Griesbaum and W. Volpp, “Reaktionen von Ozon mit 2,3-Di-tert-butyl-1,3-butadien in Lösung und auf festen Trägern,” *Chem. Ber.*, **1988**, *121*, 1795-1799. Karl Griesbaum, born 1932. University studies from 1952 at the Un. of Karlsruhe, D. phil. 1960 (Criegee). Postdoctoral Fellow Ohio State Un. (Cava) 1960-61. Research Chemist, Esso Research Eng. Center, Linden, NJ, 1961-68. Habilitation Un. Karlsruhe, 1968; Privatdozent 1968-72, Prof. Petrochem. and Org. Tech. 1972-97. Emeritus 1997. Active in ozone chemistry and other aspects of oxidation reactions and free radical chemistry..
 49. K. Griesbaum, M. Hilss, and J. Bosch, “Ozonides of Mono-, Bi- and Tricyclic Terpenes,” *Tetrahedron*, **1996**, *52*, 14813-14826.
 50. W. S. Schutt, M. E. Sigman, and Y. Li, “Fluorimetric Investigation of Reactions between Ozone and Excited state Aromatic Compounds on Silica Gel,” *Anal. Chim. Acta*, **1996**, *319*, 369-377.
 51. E. V. Avzyanova, N. N. Kabal’nova, and V. V. Shereshevovets, “Oxidation of Organic Compounds with Ozone in Adsorbed Monolayers. Part 1. Dry Ozonation of Adamantane on Silica Gel,” *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1996**, 375-378.
 52. E. V. Avzyanova, Q. K. Timerghazin, A. F. Khalizov, S. L. Khursan, L. V. Spirikhin, and V. V. Shereshevovets, “Adamantylhydrotrioxide Formation during Ozonation of Adamantane on Silica Gel,” *Mendeleev Commun.*, **1997**, 227-228.
 53. Q. K. Timerghazin, E. V. Avzyanova, A. F. Khalizov, and V. V. Shereshevovets, “Chemiluminescence during Ozonation of Adamantane on Silica Gel,” *React. Kinet. Catal. Lett.*, **1996**, *58*, 403-406.
 54. For leading references see: L. Mariey, J. Lamotte, P. Hoggan, J.-C. Lavalley, K. Boulanine, and A. Tsyganenko, “On the Basicity of Ozone,” *Chem. Lett.*, **1997**, 835-836; P. Monneyron, S. Mathe, M.-H. Manero, and J.-N Fousard, “Regeneration of High Silica Zeolites via Advanced Oxidation Processes: A Preliminary Study about Adsorbent Reactivity toward Ozone,” *Chem. Eng. Res. Des.*, **2003**, *81*, 1193-1198; M. Sugeshashi, K. Shiraishi, H. Fujita, T. Fujii, and A. Sakoda, “Ozone Decomposition of 2-Methylisoborneol (MIB) in Adsorption Phase on High Silica Zeolites with Preventing Bromate Formation,” *Water Res.*, **2005**, *39*, 3926-3934.

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THE CRUCIAL EARLY CONTRIBUTIONS OF F. R. JAPP TO A GENERAL SYNTHESIS OF IMIDAZOLE DERIVATIVES

M. John Plater, Japp Laboratory, Department of Chemistry, University of Aberdeen

Introduction

This paper explores the contributions that three authors (Japp, Radziszewski, and Debus) made to the discovery of a reaction for synthesizing imidazoles.

Radziszewski and Japp

The condensation of a 1,2-dicarbonyl compound with an aldehyde and ammonia was reported by Radziszewski (1,2). In modern times this old reaction has been exploited for library synthesis of imidazoles and has often been referred to as the Radziszewski or occasionally as the Debus-Radziszewski imidazole synthesis (3). However, another author, Francis R. Japp, played a key role in the development of this reaction (4):

We have partially investigated the action of a hydroxy-aldehyde- salicylaldehyde on phenanthraquinone in presence of ammonia, and have found that the reaction takes place according to the equation-

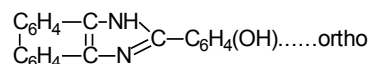


Phenanthra-	Salicyl-	New Compound
quinone	aldehyde	

The compound thus formed contains two atoms of nitrogen in the molecule, instead of one, as in the case of the compounds already described.

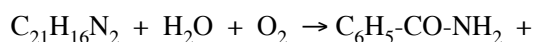
Japp published a further paper at the beginning of 1882 (5), in which he drew the structure of the product correctly as an imidazole derivative (the structure has the

hydrogen atom drawn on nitrogen and the two double bonds are drawn in the right place. In the published paper the kink in the double bond between carbon and nitrogen is not an atom).

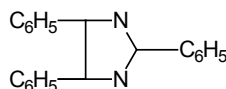


Japp's first formula for a fused imidazole

This deduction was based on a series of chemical reactions, his previous work on phenanthraquinone chemistry, and a comparison with the treatise on anhydro-bases prepared by Hübner (6) and Mensching (7). In his next paper he emphasised the pioneering structural studies on lophine reported by Fischer and Troschke (8). They reported the oxidative degradation of lophine to one equivalent of benzamide and one equivalent of dibenzamide.



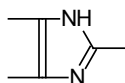
They deduced that lophine must contain three intact phenyl groups, three carbon atoms, two nitrogen atoms, and one hydrogen atom. The three carbon atoms are attached to nitrogen and for a stable ring two carbons must be attached together. Hence they arrived at a formula but were unsure of the position of the hydrogen atom and the two double bonds. The double bonds were proposed as lophine reacted with bromine.



Structure of Lophine proposed by Fischer and Troschke (the location of two double bonds and a hydrogen atom were not decided)

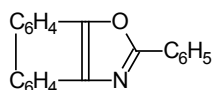
Japp also made some timely comments regarding the unusual mechanism of this reaction. Regarding the related fused oxazoles he stated (9):

We have therefore to assume that during the formation of the compounds containing one atom of nitrogen, an intramolecular rearrangement occurs: the two carbon atoms of the double keto group -CO-CO- , become united by double bonds. This corresponds with what occurs when a quinone of the ortho series-also a double ketone-is converted by the action of reducing agents into a quinol. In the present case the reducing agent is an aldehyde, and, when the aldehyde has done its work, we have no longer an aldehyde-residue, but an acid-residue in the molecule of the new compound. The occurrence of this rearrangement has been proved for three double ketones-phenanthraquinone, chrysoquinone, and benzil. As regards the compounds containing 2 atoms of nitrogen in the molecule, it seems to me that the simplest way of formulating these is to assume the existence of the complex of atoms-



...I take for granted an intramolecular rearrangement, such as occurs in the formation of the oxygenated compound.

The fused oxazole which Japp had discovered from phenanthraquinone is formed by a similar mechanism (4). The planar *cis* carbonyl groups lead to oxazole rather than imidazole products. However, oxazoles have no extra hydrogen atom on the ring, and so the two double bonds can only go in one place. Japp therefore deduced that the double bonds would go in the same place for reactions involving benzil or glyoxal, forming imidazoles. Drawing an analogy of the aldehyde to a reducing agent converting a quinone into a quinol is a beautiful idea.

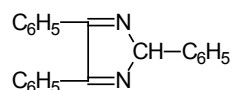


Fused oxazole

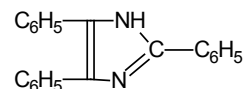
Citations are now described which lend further

credence to Japp's early contribution to this reaction. In Japp's Chemical Society paper entitled "II.-On the Constitution of Lophine (Second Notice)," he states (9):

In No.11 of the *Berichte* (**1882**, 15, 1493) (see also this journal, **1882**, Abstracts, 1063), Radziszewski communicates a new synthesis of Lophine by the interaction of benzil, benzaldehyde, and ammonia. This reaction corresponds with the synthesis of parahydroxylophine from benzil, parahydroxybenzaldehyde, and ammonia, described by Japp (*Ber.* **1882**, 15, 1268; this journal **1882**, 326). In discussing his synthesis, Radziszewski comes to the conclusion that lophine has the formula-



Radziszewski's proposal for the formula of Lophine and rejects the formula



Japp's proposal for the formula of Lophine

proposed by Mr Robinson and myself.

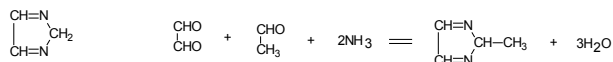
Radziszewski's deduction was in part based on the decomposition of lophine by potash into benzyl alcohol and benzoic acid, hence proceeding via benzaldehyde (1). Radziszewski's formula contains a benzaldehyde residue; Japp's formula contains a benzoic acid residue. Radziszewski however overlooked that a bis-imine formula would be hydrolytically unstable in aqueous acid. Lophine and related compounds are quite stable to acid (5). Japp proposed that a structure of his formula might hydrolyze to benzoin which might then cleave into benzaldehyde and benzoic acid to account for Radziszewski's observation.

The competitive spirit between the two scientists is evident in a further addendum published in this paper (9):

Radziszewski has published a second paper (*Ber.*, **1882**, 15, 2706), in which he describes the synthesis of Wallach's paraoxaldehyde by the interaction of glyoxal, acetaldehyde, and ammonia-here again employing a reaction belonging to the class of condensations discovered by me.

Radziszewski (1, 10) refers to Japp's earlier papers (11, 12), respectively. Japp published the correct structure

of the imidazole derivatives in all his papers, whereas Radziszewski published it incorrectly (1, 2, 10). In the first paper (1) he reports the synthesis of lophine but draws the wrong structural formula, and he reports the synthesis of imidazole or 'glyoxalin' from glyoxal and ammonia but draws the wrong structure. In his second paper (2) he describes condensing glyoxal, acetaldehyde, and ammonia to form 'paraoxalmethylin,' again reporting the incorrect structural formula. The structure of lophine in the third paper (10) is wrong. In Japp's paper (11) the structure of lophine is drawn correctly as in Ref 12.



Glyoxalin

Paraoxalmethylin

Radziszewski's proposals for 'imidazole' structures

The *Berichte* paper on Japp's work (11), which Radziszewski (1) refers to, was submitted on May 22 (Eingegangen am 22. Mai; verlesen in der Sitzung von Hrn. A. Pinner), whereas Radziszewski's paper was submitted a month later on June 19. Radziszewski's second paper was submitted later on November 17 (2).

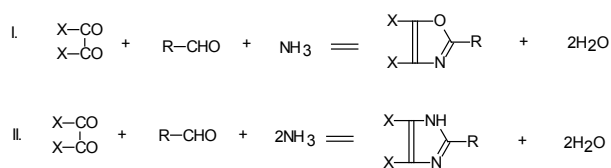
Japp followed with further papers (13, 14), in which he justified the structures as imidazole derivatives. Radziszewski's comments published in his *Chem. Soc.* paper (10), entitled "Constitution of Lophine and Allied Compounds," confirm Japp's priority in publication (10):

The author anticipates in this paper the more extended publication of the results of his investigation of this subject, in consequence of the appearance of a paper by Japp and Robinson (*Trans.*, 323) on lophine and amarine.

In other words, Japp's results (4, 5, 11, 12) were all published before Radziszewski's work appeared.

Japp's publications communicated clearly his contribution to the field. In his paper, "LIII.-On the Action of Aldehydes and Ammonia on Benzil (continued)," he states (15):

In former communications (this Journal, *Trans.*, **1880**, 666; **1881**, 225; **1882**, 146; 157, and 323; **1883**, 9 and 197, relating to the joint action of aldehydes and ammonia on compounds containing the dicarbonyl group (-CO-CO-), two general reactions of this class have been described.



[the fused oxazoles are formed from phenanthraquinone and chrysoquinone]

In Japp's paper co-authored with Wynne he states (18):

...The reactions of another dicarbonyl compound (glyoxal) with aldehydes and ammonia have, however, been studied in the case of fatty aldehydes by Radziszewski, who thus effected a new synthesis of homologues of glyoxaline (XIX-XXI). In the present communication, we describe the reactions of benzil with fatty aldehydes and ammonia.

Reactions with formaldehyde (22), acetaldehyde, isovaleraldehyde, cinnamaldehyde (which gave a different product), and aromatic aldehydes were reported by Japp. The generality of the method was developed by both scientists. According to K. Hofmann (3):

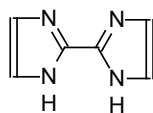
The method carries Radziszewski's name because he extended it to the preparation of simpler imidazoles and demonstrated its general applicability.

The current author believes that credit should also be given for the ring synthesis, whether substituted or unsubstituted, as it was for some other heterocycles discovered in this period (23). Japp can claim priority for (i) synthetic methods; (ii) correct structural assignment and mechanistic understanding; (iii) designation of the required components (a diketone and an aldehyde).

Debus

Prior to the above studies by Japp and Radziszewski, Heinrich Debus (1834-1916) published a single paper on this reaction (24). Both Japp and Radziszewski seem to have been unaware of it because neither refers to it. Debus reported the condensation of glyoxal with ammonia to give both imidazole and 1H,1'H-[2,2']biimidazolyl. The correct molecular formula was drawn for each, although no molecular structures were drawn. An incorrect breakdown of the molecular structure for bi(imidazole) was drawn. Imidazole is formed because a C-C bond cleavage occurs at some stage of the reaction. Radziszewski repeated the early work of Debus and reported it in his papers where he described the glyoxalin synthesis (imidazole) and proposed that glyoxal cleaves

into formaldehyde, required for the reaction, and formic acid (1, 2).



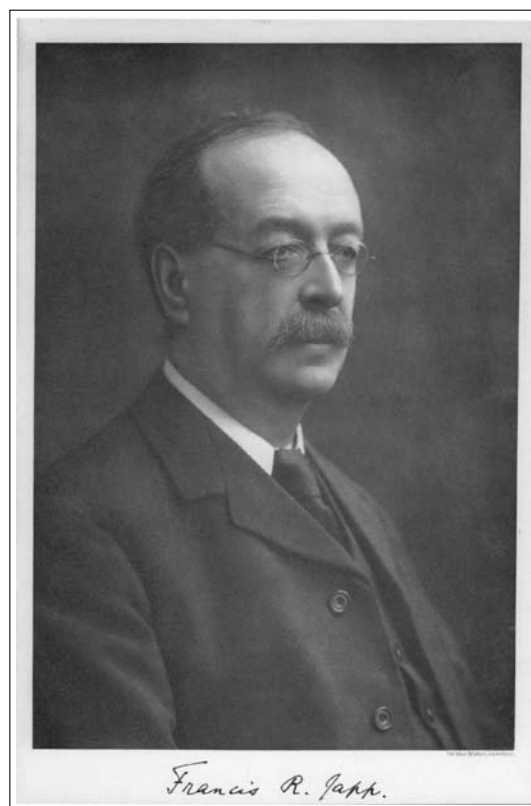
Conclusion

In conclusion Japp's group provided a significant, independent development to this reaction, which arose from a study of the condensation reactions of ammonia with phenanthraquinone. His group was the first to report the correct structure of the product as an imidazole derivative, a result contested by Radziszewski. Japp's group was the first to report the use of benzil in the reaction (11, 12), work cited in two of Radziszewski's papers (1, 10). Japp showed that diketones other than glyoxal could be used. He published a mechanistic rationale for the reaction, proposing that the aldehyde acts as a reducing agent on the diketone and that an intramolecular rearrangement leads to the product (9). Most importantly, Japp was the first to show that a 1,2-diketone could be used along with a separate aromatic or aliphatic aldehyde, to effect the reaction. This opened up the scope of the reaction that is exploited today and is a significant step following from Debus's original discovery of the synthesis of the parent imidazole. The Japp group published four papers (4,5,11,12) on the imidazole-forming reaction before the Radziszewski group had published any. Interestingly, neither author grasped that Japp's structural formula is more stable because of aromaticity (25). A number of new heterocyclic ring systems were discovered in this decade, but substituted derivatives were sometimes prepared, such as pyrrole and pyridine derivatives, and served to give the authors inventorship (23). For Japp to claim that it was a "class of condensations discovered by me" is, however, a stretch of the truth (9)!

REFERENCES AND NOTES

- B. Radziszewski, "Ueber die Constitution des Lophins und verwandter Verbindungen" *Ber. Dtsch. Chem. Ges.* **1882**, *15*, 1493-1496.
- B. Radziszewski, "Ueber Glyoxalin und seine Homologe" *Ber. Dtsch. Chem. Ges.*, **1882**, *15*, 2706-2708.
- Some examples: D. R. J. Acke, R. V. A. Orru, and C. V. Stevens, "Continuous Synthesis of Tri- and Tetrasubstituted Imidazoles via a Multicomponent Reaction under Microreactor Conditions" *QSAR & Comb. Sci.*, **2006**, *25*, 474-483; K. Hofmann in A. Weissberger, Ed., *Imidazole and its Derivatives*, Interscience Publishers, New York, Chapter II, "The Alkyl- And Arylimidazoles" 1953, 33; Y. Ogata, A. Kawasaki and F. Sugiura, "Kinetics of the formation of triphenylimidazoles from benzils," *J. Org. Chem.*, **1969**, *34*, 3981-3985; A. Domling and I. Ugi, "Multicomponent reactions with isocyanides," *Angew. Chem. Int. Ed. Engl.*, **2000**, *39*, 3168-3210; K. Matsumoto, J. Chul Kim, H. Iida, H. Hamana, K. Kumamoto, H. Kotsuki, and G. Jenner, "Multicomponent Strecker Reaction under High Pressure" *Helv. Chim. Acta.*, **2005**, *88*, 1734-1753; J. Andraos, "Unification of Reaction Metrics for Green Chemistry II: Evaluation of Named Organic Reactions and Application to reaction Discovery," *Org. Process Res. Dev.*, **2005**, *9*, 404-431; D. O. Tymoshenko, "On the development of organic chemistry in Ukraine," *ARKIVOC*, **2005**, *viii*, 1-3; M. Kidwai, S. Saxena, Ruby and S. Rastogi, "An Efficient Synthesis of 2,4,5-Trisubstituted and 1,2,4,5-Tetrasubstituted 1H-imidazoles," *Bull. Korean Chem. Soc.*, **2005**, *26*, 2051-2053; N. J. Curtis and R. S. Brown, "An Easily Introduced and Removed Protecting Group for Imidazole Nitrogen: a Convenient Route to 2-Substituted Imidazoles," *J. Org. Chem.*, **1980**, *45*, 4038-4040; J. Wolff and I. Covelli, "Factors in the Iodination of Histidine in Proteins" *Eur. J. Biochem.*, **1969**, *9*, 371-377; E. Gelens, F. J. J. De Kanter, R. F. Schmitz, L. A. J. M. Sliedregt, B. J. Van Steen, C. G. Kruse, R. Leurs, M. B. Groen, and R. V. A. Orru, "Efficient Library Synthesis of Imidazoles using a Multicomponent Reaction and Microwave Irradiation," *Mol. Div.*, **2006**, *10*, 17-22.
- F. R. Japp, "On the Action of Aldehydes on Phenanthraquinone in Presence of Ammonia. (Second Notice)," *J. Chem. Soc., Trans.*, **1881**, *39*, 225-228.
- F. R. Japp and F. W. Streatfeild, "On the Action of Aldehydes on Phenanthraquinone in Presence of Ammonia. (Third Notice)," *J. Chem. Soc., Trans.*, **1882**, *41*, 146-156.
- H. Hübner, "Ueber Anhydroverbindungen" *Liebigs Ann. Chem.*, **1881**, *210*, 328-396.
- C. Mensching, "Nitrirung von Salicylanilid,," *Ber. Dtsch. Chem. Ges.*, **1880**, *13*, 462-463.
- E. Fischer and H. Troschke, "Ueber Amarin und Lophin," *Ber. Dtsch. Chem. Ges.*, **1880**, *13*, 706-711.
- F. R. Japp, "II.-On the Constitution of Lophine (Second Notice)," *J. Chem. Soc., Trans.*, **1883**, *43*, 9-18.
- B. Radziszewski, "Constitution of Lophine and Allied Compounds," *J. Chem. Soc., Trans.*, **1882**, *43*, 1063-1065.
- F. R. Japp and H. H. Robinson, "Constitution des Lophins und des Amarins," *Ber. Dtsch. Chem. Ges.*, **1882**, *15*, 1268-1270.
- F. R. Japp, "L.- On the Constitution of Amarine and Lophine" *J. Chem. Soc., Trans.*, **1882**, *41*, 323-329.
- F. R. Japp, "Constitution des Lophins, des Amarins und des Glyoxalins," *Ber. Dtsch. Chem. Ges.*, **1882**, *15*, 2410-2421.

14. F. R. Japp, "On Condensations of Compounds which contain the Dicarboxyl group with Aldehydes and Ammonia," *J. Chem. Soc., Trans.*, **1883**, 43, 197-200.
15. F. R. Japp and S. C. Hooker, "On the Action of Aldehydes and Ammonia on Benzil (continued)," *J. Chem. Soc., Trans.*, **1884**, 45, 672-685.
16. F. R. Japp, "LVIII.-On the Action of Benzaldehyde on Phenanthraquinone, both alone and in presence of Ammonia" *J. Chem. Soc., Trans.*, **1880**, 37, 661-672.
17. F. R. Japp and F. W. Streatfeild, "XXIV. Application of the Aldehyde and Ammonia Reaction in Determining the Constitution of Quinones," *J. Chem. Soc., Trans.*, **1882**, 41, 157-159.
18. F. R. Japp and W. Palmer Wynne, "XLVI. On the Action of Aldehydes and Ammonia on Benzil (continued)," *J. Chem. Soc., Trans.*, **1886**, 49, 462-472.
19. B. Radziszewski, "Ueber die Synthese der Oxalinbasen," *Ber. Dtsch. Chem. Ges.*, **1883**, 16, 487-494.
20. B. Radziszewski, "Ueber einige neue Glyoxaline," *Ber. Dtsch. Chem. Ges.*, **1883**, 16, 747-749.
21. B. Radziszewski and L. Szul, "Ueber das Glyoxal-isoamylin und dessen Abkömmlinge," *Ber. Dtsch. Chem. Ges.*, **1884**, 17, 1291-1296.
22. F. R. Japp, "Diphenylglyoxaline and Methyl-diphenylglyoxaline," *J. Chem. Soc., Trans.*, **1887**, 51, 557-564.
23. 1880-1890 was an exciting period for the discovery of new heterocyclic syntheses. These include the Skraup; "Eine Synthese des Chinolins," *Ber. Dtsch. Chem. Ges.*, **1880**, 13, 2086-2089 and Doebner-Von Miller, "Ueber eine dem Chinolin homologe Base," *Ber. Dtsch. Chem. Ges.*, **1881**, 14, 2812-2817; quinoline syntheses; the Knorr pyrrole synthesis "Synthese von Pyrrolderivaten," *Ber. Dtsch. Chem. Ges.*, **1884**, 17, 1635-1642; the Paal; "Synthese von Thiophen- und Pyrrolderivaten," *Ber. Dtsch. Chem. Ges.*, **1885**, 18, 367-371; Knorr "Einwirkung des Diacetbernsteinsäure-esters auf Ammoniak und primäre Aminbasen," *Ber. Dtsch. Chem. Ges.*, **1885**, 18, 299-311; pyrrole synthesis and the Hantzsch pyridine synthesis; "Condensationsproducte aus Aldehydammoniak und ketonartigen Verbindungen," *Ber. Dtsch. Chem. Ges.*, **1881**, 14, 1637-1638.
24. H. Debus, "Ueber die Einwirkung des Ammoniaks auf Glyoxal," *Ann. Chem. Pharm.*, **1858**, 107, 199-208.
25. The structure of benzene as a cyclohexatriene was drawn by Kekulé, "On some Condensation-products of Aldehyde," *J. Chem. Soc.*, **1872**, 25, 612-619; "Ueber einige Condensationsproducte des Aldehyds," *Ann. Chem. Pharm.*, **1872**, 162, 77-124; and a representation beforehand, "Sur la constitution des substances aromatiques," *Bull. Soc. Chim. Fr.*, **1865**, 3, 98-110.



Francis R. Japp

Francis Robert Japp (1845-1925)

Born and schooled in Dundee, Japp graduated M.A. (Arts) from St Andrews University in 1868 and proceeded to Edinburgh University to study Law. Ill health terminated his studies prematurely, and while recuperating in Germany he committed himself to the study of chemistry. He was a student of Bunsen and Kopp at Heidelberg (D. Phil. 1875) and Kekulé in Bonn before returning to Scotland to work with Crum-Brown in Edinburgh. After a lengthy period with Frankland in London at the Royal College of Science, he was appointed to the Chair of Chemistry in Aberdeen in 1890. There he created a school of chemistry where previously chemistry had been taught mainly in support of medicine; and by 1896 he had persuaded the University to provide new and much improved facilities for the study of chemistry.

His research work concerned mainly diketones and especially their condensation with ammonia, amines, and nitriles. This led to the isolation of many heterocycles such as imidazoles, indoles, and oxazoles, whose properties and structures were examined. Details of this work can be found in the *Journal of the Chemical Society* during the period 1880-1906. This work was recognized by his election as Fellow of the Royal Society, Vice-

President of the Chemical Society, Royal Institute of Chemistry, and British Association (Chemistry Section) and the award of the Longstaff Medal and honorary degrees from the University of St Andrews and the University of Aberdeen.

Bronislaus Radziszewski (1838-1914)

Radziszewski was born in 1838 in Warsaw and graduated

from Moscow University in 1861. He was a teacher for some time in Warsaw, after which he studied with Kekulé in Gent, Belgium, from 1864-1867. He worked for two years with L. Henry in Lowen, Belgium. From 1870-72 he was professor at the Technical Institute in Kraków, Poland



Bronislaus Radziszewski

and was Professor of

Chemistry at Lwow University (formerly Austro-Hungarian Empire and now L'viv University, Ukraine) for 38 years until he retired in 1911. He founded the Lwow

school of organic chemistry, held the first chair of organic chemistry from 1895-1911, and was rector from 1882-1883. The author of 340 publications, he was a member of the Kraków Academy of Arts and Sciences. Among his many chemical pursuits he discovered a method to synthesize carbonic acid amides by treating nitriles with hydrogen peroxide in base.

ABOUT THE AUTHOR

Dr M. John Plater, Japp Laboratory, Department of Chemistry, University of Aberdeen, Meston Walk, Aberdeen, AB24 3UE UK [m.j.plater@abdn.ac.uk], graduated from Loughborough University with a B.Sc. in chemistry and obtained a Ph.D. from Imperial College of Science, Technology and Medicine, working with Charles Rees on sulfur-nitrogen chemistry. After a research fellowship for one year at Columbia University with Clark Still, he was appointed as lecturer in chemistry at Aberdeen University. He was promoted to senior lecturer in 1998. His nearly 80 publications cover a broad range of topics including free radicals, heterocyclic ligands, and solid phase synthesis, as well as the conservation of art, prebiotic chemistry, and the history of science. A full list of publications can be found on his website [<http://www.abdn.ac.uk/chemistry/research/mjp/mjp.shtml>].

WEBSITES

HIST: <http://www.scs.uiuc.edu/~mainzv/HIST>

CHEMICAL HERITAGE: <http://www.chemheritage.org>

HISTORY OF SCIENCE SOCIETY: <http://www.hssonline.org>

FROM DISULFIRAM TO ANTABUSE: THE INVENTION OF A DRUG

Helge Kragh, University of Aarhus

Introduction

Antabuse® is the trade name for an organic sulfur compound, chemically identical to disulfiram or tetraethylthiuram disulfide, a light-gray crystalline powder with a molecular weight of 296.54. In 1945 Danish researchers observed that the substance caused very unpleasant physiological effects in persons who had consumed alcohol. A few years later this chance observation was turned into a profitable production of pills used to combat alcoholism (antabuse = anti-abuse). The new drug quickly came into general use in Denmark and also, if somewhat later and on a lesser scale, internationally.

While the literature on the biochemical and medical aspects of antabuse or disulfiram is massive (1), almost nothing has been written about its discovery and subsequent history. This paper focuses on the innovative phase in the period between 1945 and the early 1950s. How was the peculiar effect of disulfiram discovered? How was it turned into a marketable drug? What were the early clinical experiences?

To the extent that the discovery story of antabuse is known, it is probably because it is a typical case of serendipity, an unintended discovery made in a research process with a different goal (2). Most Americans would first have known of the new drug from an article titled "Drug for Drunks" in *Time* of December 6, 1948. "The discovery was an accident," according to the article, and the writer continued (3):

Copenhagen's Dr. Erik Jacobsen, 45, likes to try out new drugs on himself before giving them to his patients. One night before going to a dinner party he swallowed a couple of pills made of tetraethylthiuram-disulfide; they were supposed to be good for intestinal worms. To his surprise, Dr. Jacobsen found that any form of alcohol revolted him. When he sipped even a small glass of beer, his face got red, his heart started to pound, and he had trouble getting his breath.

Other accounts of this example of self-experimentation are more dramatic if not necessarily more authentic. Thus, according to a recent book, at one point, "Jacobsen's blood pressure fell to almost zero and he came close to death" (4). This incident happened after Jacobsen had taken a pill of disulfiram and subsequently had alcohol injected intravenously.

Disulfiram before 1945

Whereas antabuse dates from 1948, disulfiram goes farther back in history. A Berlin chemist, M. Grodzki, reported in 1881 that he had synthesized a new compound from thiocarbamide and that its stoichiometric formula was $C_{10}H_{20}N_2S_4$ (5). His report, published in *Berichte*, caused little attention. This was the heyday of organic synthesis, when chemists—and German chemists in particular—produced one new compound after the other. Grodzki's seemed to be just one more.

However, some twenty years later, disulfiram was introduced in the developing rubber industry to accelerate the vulcanization of rubber (6). The substance proved effective and was widely used in the vulcanization of both natural rubber and synthetic rubber products such as neoprene. It was in connection with the rubber industry that a possible connection between disulfiram and the ingestion of alcohol was first noticed. In 1937 E. E. Williams, a plant physician in the American rubber industry, described how workers in the plant, processing tetramethylthiuram monosulfide and disulfide, suffered trouble when ingesting alcohol (7). Williams thought that the adverse properties of disulfiram and related compounds to alcohol might perhaps lead to "the cure for alcoholism," but neither he nor others followed up the suggestion. The effect of disulfiram on intake of alcohol was also known in the Swedish rubber boot industry, without any one in Sweden suggesting its possible use as a drug against alcoholism (8).

It is also relevant to point out that since the early years of the twentieth century it had been known that cyanamides produce hypersensitivity to alcohol in workers in the cyanamide industry. In this industry, based on the Frank-Caro process, atmospheric nitrogen was transformed into calcium cyanamide, which is used as a fertilizer. The effect was first described by a German physician in 1914 and subsequently verified by other studies, but the causal mechanisms remained unknown; nor does anyone seem to have thought of cyanamide as a possible therapeutic agent in combating alcoholism.

Apart from its use in the rubber industry, from the early 1940s disulfiram was also used in medicine as a scabicide. In 1942 two British physicians concluded that tetraethylthiuram monosulfide was a promising drug against scabies (9). The effect of the disulfide in destroying scabies, and possibly also intestinal worms, was investigated by Swedish pharmacologists, among others, who used disulfiram to cure domestic animals for scabies (10). The findings of the Swedish researchers were received with interest in Copenhagen, where the chemical company Medicinalco Inc. wanted to establish its own production of a disulfiram ointment capable of curing scabies. If the product could also be used as a vermicide, so much the better.

The Discovery of Antabuse

Trained as a physician, Erik Jacobsen (1903-1985) specialized in biochemistry and worked from 1932-34 at Copenhagen University's biochemical institute, founded in

1928. In 1934 the 31-year old Jacobsen became head of the pharmaceutical company Medicinalco's biological-chemical laboratory, a center for biomedical research in the Copenhagen area. After having served industry in this position for nearly twenty years, he was appointed in 1962 professor of pharmacology at the Pharmaceutical College, an institution established in 1892 and recently merged with the University of Copenhagen.

During the German occupation of Denmark (1940-45), Jacobsen became interested in problems of cell oxidation, which he discussed with Jens Hald, a pharmacologist and experienced analytical chemist, who was associated with Medicinalco's laboratory and involved in research on the copper metabolism of intestinal worms. Jacobsen and Hald realized that the scabicide effect of disulfiram was due to its ability to absorb copper and form chelates with the metal. (It was known that in lower forms of life oxygen is transported by copper and not, as is the case in vertebrates, by iron.) They consequently reasoned that the drug would probably work also for intestinal worms, which at the time was a widespread nuisance not only for animals but also for children. Experiments with rabbits confirmed their suspicion that disulfiram was effective as a vermicide, leaving the substance to be tested also for intestinal worms in humans.

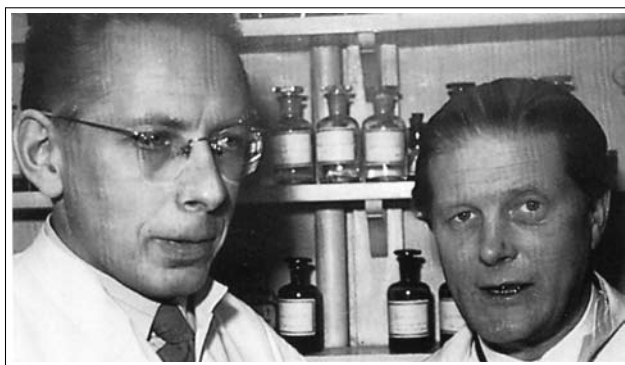


Figure 1. Jacobsen (right) and Hald in Medicinalco's Laboratory, about 1950.

What happened next was Jacobsen's decision to evaluate possible side-effects on himself, such as recounted in the article in *Time*. Hald had experienced a similar but weaker reaction, and the two researchers therefore suspected that the combined presence of disulfiram and alcohol was responsible. Jacobsen recalled (11):

It only took a few days to confirm that the disulfiram tablets really changed the effect of alcohol in a most unpleasant direction.

In the spring of 1945 Hald, Jacobsen, and their collaborators at Medicinalco vaguely realized that disulfiram might be used as a drug for alcohol treatment, but at the time they did not follow up the idea. They seem to have believed that alcoholism was not a major problem in Danish society and that an alcohol-deterrent drug was therefore of little commercial interest.

It was only two years later that the situation changed, mainly a result of the contact established in the fall of 1947 between Jacobsen and Oluf Martensen-Larsen, a physician who had experience with treatment of alcoholics. Collaborating with Martensen-Larsen, Hald and Jacobsen now initiated systematic studies in order to develop a disulfiram-based drug, to understand its physiological actions, and to establish its efficiency in clinical trials. Experiments confirmed that the disulfiram-ethanol reaction mainly took place in the liver, the most important organ capable of oxidizing ingested alcohol. As to the pharmacological actions of disulfiram, Hald and Jacobsen realized the crucial importance of acetaldehyde. According to Jacobsen's recollections nearly thirty years later (12):

One of our collaborators, a chemist, happened to enter the laboratory and pointed out the strong smell of acetaldehyde. We, being present in the room, had not noticed the smell because we had slowly adapted to it. This observation gave us the key to understand the process. Further experiments proved that when acetaldehyde was injected intravenously it resulted in the same symptoms as previously experienced. Enzymatic experiments proved that the oxidation of acetaldehyde, the first step in the oxidation chain of ethanol, was impeded by disulfiram in concentrations 1 : 10⁷.

One more accidental observation paved the way for antabuse. A sample of disulfiram had accidentally been polluted with small amounts of copper, and Jacobsen and his group noticed that the dark precipitate did not disappear by following the standard procedure of washing with ethanol. They succeeded in removing the precipitate by recrystallizing with carbon tetrachloride and in this way also securing a better drug. After the solvent had evaporated, disulfiram was left in a state with a much larger surface and therefore more easily absorbed in the organism. This form of disulfiram, named antabuse (or "antabus" in Danish), was granted a Danish patent in 1952, with patent protection retroactive from 1949 (13). The Danish version of the name was initially used also by English and American authors, but it was soon transformed into the Anglicized version.

Disseminating a Drug

The discovery of antabuse, meaning the effect of disulfiram in preventing intake of alcohol, was announced to an international audience in an invited lecture Jacobsen gave to the annual meeting of the British Pharmacological Society on July 9, 1948. The following fall he and his group of researchers were busy with extending their studies of the many aspects of the disulfiram-ethanol reaction and publishing their results. Their productivity in 1948-49 was impressive.

The most important journal for the dissemination of knowledge concerning the actions of antabuse in the organism was the *Acta Pharmacologica et Toxicologica*, an international journal founded in 1945 and edited by Scandinavian scientists. The fact that it was published in Copenhagen and that Jacobsen was among the editors made it an ideal journal for publishing new research related to antabuse. For example, Vol. 4 of 1948 included two substantial papers by Hald and Jacobsen on the formation and action of acetaldehyde; and their collaborator Erik Rasmussen, a pharmacologist associated with Medicinalco, reported his investigations of the action of the antabuse-alcohol reaction on the blood circulation and respiration (14).



Figure 2. One of the early issues of *Acta Pharmacologica et Toxicologica*, the favorite journal of antabuse research.

Hald and Jacobsen measured the small amount of acetaldehyde in the blood of individuals treated with antabuse by means of a color reaction with *p*-hydroxydiphenyl. In order to be certain that the increase found was really due to acetaldehyde, and not to some other substances giving a similar reaction, they isolated and identified chemically acetaldehyde in the expired air. This they did by isolating and weighing the red-brown crystals of the derivative formed with an acid solution of 2,4-dinitrophenylhydrazine. In their study of 1948 Hald and Jacobsen demonstrated in this way an eightfold increase in aldehyde concentration in blood when 40 ml of alcohol was consumed after 1.5 g of antabuse was taken the previous day.

The medical world learned about antabuse by way of two companion papers by Jacobsen and Martensen-Larsen that appeared in *The Lancet* in December, 1948. According to Jacobsen's summary (15):

Alcohol given to persons previously treated with this otherwise innocuous substance produces dilatation of the facial vessels, increased pulmonary ventilation, raised pulse-rate, and general uneasiness. The symptoms appear to be the result of an increased formation of acetaldehyde from alcohol.

Martensen-Larsen reported on his clinical treatment of 83 patients in the period from December, 1947 to May, 1948. Since more than half of the patients benefited markedly from the treatment, he concluded that it was "promising." On the other hand, he fully realized that it could not stand alone. "The treatment with antabuse must often be only part of a general treatment," he emphasized (16).

This was also the conclusion of American and Canadian physicians who had followed the news from Copenhagen with great interest and conducted their own investigations. Erik Glud, a young Danish physician who was a resident in 1949 at the New Haven (CT) Hospital, wrote an article on the antabuse cure specifically addressed to American physicians. As he pointed out, because American drinking patterns were different from those in Scandinavia, the Danish treatment with antabuse needed to be modified before it was introduced in the United States (17).

At the annual meeting of the American Psychiatric Association, taking place in Montreal in May, 1949, three physicians from Albany (NY) Hospital described their antabuse treatment of 21 patients, all habitual drinkers, over a period of two to four months. As a result of the treatment, 14 of the patients discontinued the use of

alcohol entirely. "It is important to emphasize," they wrote, "that the chief value of Antabuse lies in the fact that it paves the way for psychotherapeutic procedures. ... Antabuse in conjunction with psychotherapy may prove superior to other methods of treatment of chronic alcoholism" (18).

The Metabolism of Ethanol

Investigations of the action of antabuse and the fate of ethanol in the organism became a major research topic among the group of scientists in Copenhagen associated with Jacobsen and Hald. Whereas some of them focused on the clinical aspects, others studied the biochemical and pharmacological aspects. For example, Knud Raby, a young medical researcher, studied the disulfiram-ethanol reaction from a clinical point of view; and Erling Asmussen, a sports physiologist, did research on the pharmacological action of the acetaldehyde accumulated by the presence of antabuse (19).

Jacobsen occupied himself in particular with the metabolism of ethanol, a topic that attracted much attention at the time. In 1952 he published a comprehensive review of all aspects of the subject, and in January of that year he delivered an invited lecture on the topic at University College, London (18). The scientific study of ethanol's fate in the organism was of course not new. Important research had been done in the 1920s and 1930s, in particular by the Swedish chemist Erik Widmark, a pioneer of forensic medicine and chemistry (21). It had been established that the combustion of practically all ethanol takes place in the liver, and that the enzymatic oxidation to acetic acid occurs with acetaldehyde as an intermediate:



However, little was known of the reaction mechanisms or about substances that either promoted or inhibited the processes.

According to the new investigations, as undertaken in Copenhagen and elsewhere, ethanol is oxidized to acetaldehyde by means of the enzyme alcohol dehydrogenase (ADH); the acetaldehyde is subsequently transformed to acetic acid by the action of another enzyme, aldehyde dehydrogenase (ALDH). The principal action of antabuse is to block the action of ALDH, with the result of an accumulation of acetaldehyde (22):

"Antabuse" inhibits the flavin-containing aldehyde oxidases, and the aldehyde dehydrogenase, of the

organism. *In vitro* concentrations about $1/10^7$ give a marked inhibition of the enzymatic actions, and the degree of inhibition is diminished with increasing concentrations of the substrates, suggesting a competition between “Antabuse” and aldehyde for the enzyme.

Among the first to establish the action of antabuse as an inhibitor for ALDH was Niels Ole Kjeldgaard, a 23-year old graduate student and later professor of molecular biology. In a series of experiments beginning in 1949 Kjeldgaard demonstrated that even in concentrations as small as $0.1 \mu\text{g/ml}$ antabuse exerted a strong inhibition on the oxidation to acids by the liver aldehyde oxidases (23).

Among the results obtained by Jacobsen and his associates was the conclusion that a much larger dose of antabuse is required to block the transformation of ethanol to acetaldehyde than for the subsequent transformation to acetic acid. Even if the first process is impeded almost completely, it will not affect the transformation of aldehyde. Hald and his collaborator Valdemar Larsen, a pharmacologist, further found that other substances besides disulfiram act as inhibitors for the acetaldehyde-acetic acid process. It had been known for some time that cyanamide provoked disagreeable symptoms in combination with alcohol, and Hald and Larsen established that similar effects were produced by tetraethylthiuram monosulfide, tetramethyl disulfide, and a few other compounds similar to disulfiram (24).

The discovery of antabuse stimulated not only research in the metabolism of ethanol, but also other areas of a related chemical, pharmacological, and clinical nature. On the basis of a perusal of review papers and bibliographies, it is estimated that during the period 1948-53 about 140 research papers were written on antabuse and its effects; of these, about 40 were written

by Danish scientists and physicians. The research effort was of course international, involving scientists from the Scandinavian countries, the United States, Great Britain, Switzerland, Portugal, France, South Africa, Canada, and Austria.

Uses of Disulfiram

Treatment of alcoholism with antabuse was quickly introduced in the Scandinavian countries. In Denmark and Sweden, the drug was approved for medical prescriptions in early 1949 and generally looked upon with high expectations. In spite of the cautious attitude of many

physicians, the public tended to see antabuse – or abstynyl, as its equivalent was named in Sweden – as a kind of wonder drug. “Antabuse on its triumphant march throughout the world” read a headline in the Swedish newspaper *Dagen* of October 17, 1949.

Although the initial optimism soon waned, by the mid 1950s it had become the dominant procedure for treating alcohol misuse in the Danish health system. Antabuse was, and still is, to a large extent considered a “Danish drug” (25). There are a few other drugs with a similar effect (naltrexone and acomprosate), but these are only prescribed very rarely by Danish physicians. In the beginning

of the 21st century the total prescriptions per year in Denmark was 5 million daily doses, corresponding to an estimated number of 25,000 patients. The number of persons treated with naltrexone or acomprosate is less than 1,000.

In the United States antabuse was approved by the Federal Drug Administration in 1951, followed by approval of naltrexone in 1994 and acomprosate in 2004. According to a recent study, there are only about 250,000 disulfiram prescriptions (antabuse or some other brand)

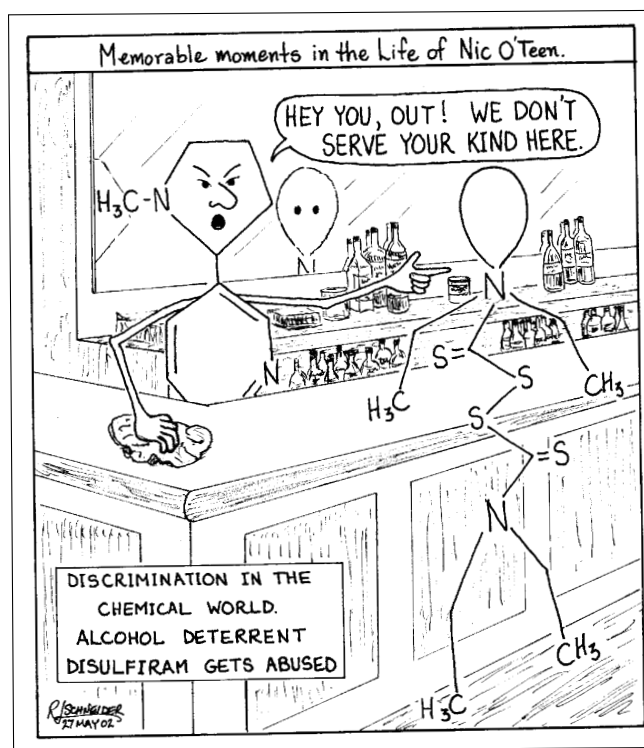


Figure 3. Cartoon by Roger L. Schneider, from Amalgamator website (<http://alchemy.chem.uwm.edu/amalgamator/cartoons/>). Reproduced with permission of the artist.

written per year in the United States for treatment of alcoholism (1). Neither in the United States nor elsewhere is antabuse used on the same scale as in its country of origin. It is estimated that some 120,000 persons throughout the world take antabuse against their misuse of alcohol. About twenty per cent of them are from Denmark, a country of 5.3 million inhabitants.

The discovery of antabuse in 1948 stimulated research in therapeutic properties of disulfiram other than those related to preventing excessive drinking. As early as 1951, a research group under Henrik Dam found that antabuse had a beneficial effect on symptoms caused by a lack of vitamin E (26). A Nobel laureate of 1944 for his discovery of vitamin K, Dam served at the time as professor of biochemistry at Denmark's Technical University. While he continued his studies of vitamin K, in the early 1950s his main field of research was the nutritional and other effects of vitamin E (27). Dam's studies were further developed by the Danish odontologist Jens Pindborg, who, while working as a consultant for Medicinalco, showed that certain dental diseases caused by lack of vitamin E could be cured by disulfiram (28). Much research has recently been done on the therapeutic properties of the compound. It appears to have a significant potential in the treatment of human cancers and certain drug-resistant fungal infections (29).

Presently there is a strong focus on disulfiram's role in the treatment of cocaine addiction, both among patients who are alcohol-dependent and those who are not. According to Kathleen Carroll and her colleagues, the effect of disulfiram is not restricted to cocaine abusers who are also misusers of alcohol. On the contrary (30):

...disulfiram therapy might, paradoxically, be particularly appropriate for the treatment of cocaine problems among drug users who are not regular or problematic drinkers.

REFERENCES AND NOTES

- J. J. Suh, H. M. Pettinati, K. M. Kampman, and C. P. O'Brien, "The Status of Disulfiram, a Half of a Century Later," *J. Clin. Psychopharm.*, **2006**, *26*, 290-302.
- R. M. Roberts, *Serendipity: Accidental Discoveries in Science*, John Wiley, New York, 1989. M. A. Meyers, *Happy Accidents: Serendipity in Modern Medical Breakthroughs*, Arcade Publishing, London, 2008.
- Time*, December 6, 1948; see also *Time*, January 10, 1949 and January 31, 1949.
- Ref. 2 (Meyers), p 285; L. K. Altman, *Who Goes First? The Story of Self-Experimentation in Medicine*, Random House, New York, 1986, 103.
- M. Grodzki, "Über äthylirte Sulfoharnstoffe," *Ber. Dtsch. Chem. Ges.*, **1881**, *14*, 2754-2758.
- D. Twiss, S. A. Bazier, and F. Thomas, "The Dithiocarbamate Accelerators of Vulcanization," *J. Soc. Chem. Ind.*, **1922**, *41*, 81T-88T.
- E. E. Williams, "Effects of Alcohol on Workers with Carbon Disulfide," *J. Am. Med. Assoc.*, **1937**, *109*, 1472-1473.
- S. Eriksen, "From Gold Cure to Antabuse: Danish Treatment Traditions in a Liberal Drinking Culture," in J. Erdman and K. Stenius, Ed., *On the Margin: Nordic Alcohol and Drug Treatment 1885-2007*, Nordic Center for Alcohol and Drug Research, Oslo, 2008, 51-79 (75).
- R. M. Gordon and D. R. Seaton, "Observations on the Treatment of Scabies," *Brit. Med. J.*, **1942**, *1*, No. 4248, 685-687.
- S. Hammarskjöld, "Tenurid – ett Nytt Skabbmedel," *Svenska Läkartidningen*, **1943**, *40*, 2813-2814; G. Hagerman and M. Tottie, "Tetraethyl-Monosulfid, ett Nytt Medel mot Skabb," *Svenska Läkartidningen*, **1943**, *40*, 2815-2818.
- E. Jacobsen, "Et Præparat Fødes," *Medicinsk Forum*, **1958**, *11*, 180-184 (181).
- E. Jacobsen, "Nogle Tilfældige Opdagelser i Farmakologien," *Dansk Kemi*, **1977**, *58*, 58-67 (66).
- Danish Patent No. 73997 of March 31, 1952. According to Danish patent law at that time, a drug could not be patented, only methods to produce it.
- J. Hald and E. Jacobsen, "The Formation of Acetaldehyde in the Organism after Ingestion of Antabuse (Tetraethylthiuramdisulphide) and Alcohol," *Acta Pharm. Tox.*, **1948**, *4*, 305-310; J. Hald, E. Jacobsen, and V. Larsen, "The Sensitizing Effect of Tetraethylthiuramdisulphide (Antabuse) to Ethyl Alcohol," *Acta Pharm. Tox.*, **1948**, *4*, 285-296; E. Rasmussen, "Studies on the Effect of Tetraethylthiuramdisulphide (Antabuse) and Alcohol on Respiration and Circulation in Normal Human Subjects," *Acta Pharm. Tox.*, **1948**, *4*, 297-304.
- J. Hald and E. Jacobsen, "A Drug Sensitising the Organism to Ethyl Alcohol," *The Lancet*, **1948**, *252*, 1001-1004.
- O. Martensen-Larsen, "Treatment of Alcoholism with a Sensitising Drug," *Lancet*, **1948**, *252*, 1004-1005.
- E. Glud, "The Treatment of Alcoholic Patients in Denmark with 'Antabuse'; with Suggestions for its Trials in the United States," *Quart. J. Stud. Alcohol*, **1949**, *10*, 185-197.
- E. Barrera, W. Osinski, and E. Davidoff, "The Use of Antabuse (Tetraethylthiuramdisulphide) in Chronic Alcoholics," *Am. J. Psychiatry*, **1950**, *107*, 8-13; reprinted in the same journal, **1994**, *151*, 263-267. For a somewhat similar study at St. Patrick's Hospital, Dublin, see J. Moore and M. Drury, "Antabus in the Management of Chronic Alcoholism," *Lancet*, **1951**, *258*, 1059-1061; see also F. Gelbman and N. B. Epstein, "Initial Clinical

- Experience with Antabuse," *J. Can. Med. Assoc.*, **1949**, 60, 549-552.
19. K. Raby, "Investigations on the Disulfiram-Alcohol Reaction: Clinical Observations," *Quart. J. Stud. Alcohol*, **1953**, 14, 545-556; K. Raby, "Investigations of the Acid-Base Balance of the Blood during the Disulfiram-Alcohol Reaction," *Quart. J. Stud. Alcohol*, **1954**, 15, 207-216; E. Asmussen, "The Pharmacological Action of Acetaldehyde on the Human Organism," *Acta Pharm. Tox.*, **1948**, 4, 311-315.
 20. E. Jacobsen, "The Metabolism of Ethyl Alcohol," *Pharm. Rev.*, **1952**, 4, 107-135; E. Jacobsen, "The Metabolism of Ethyl Alcohol," *Nature*, **1952**, 169, 645-647.
 21. R. Andreasson and A. W. Jones, "The Life and Work of Erik M.P. Widmark," *Am. J. For. Med. Path.*, **1996**, 17, 177-190.
 22. Ref. 20 (*Nature*), p 646.
 23. N. O. Kjeldgaard, "Inhibition of Aldehyde Oxidase from Liver by Tetraethylthiuramdisulphide (Antabuse)," *Acta Pharm. Tox.*, **1949**, 5, 397-403.
 24. E. Hald og V. Larsen, "The Rate of Acetaldehyde Metabolism in Rabbits Treated with Antabuse (Tetraethylthiuramdisulphide)," *Acta Pharm. Tox.*, **1949**, 5, 292-297.
 25. H. Thiesen, "Conservatism and Social Control: Treatment with Disulfiram in Denmark, 1945-2005," in J. Erdman and K. Stenius, Ed., *On the Margin: Nordic Alcohol and Drug Treatment 1885-2007*, Nordic Center for Alcohol and Drug Research, Oslo, 2008, 121-137.
 26. E. Aas-Jørgensen, H. Dam, and H. Granados, "The Influence of Antabuse (Tetraethylthiuram Disulphide) and Methylene Blue on Certain Vitamin E Deficiency Symptoms and on Growth in Rats," *Acta Pharm. Tox.*, **1951**, 7, 171-180.
 27. H. Kragh and M. K. Møller, "Henrik Dam: The Anonymous Laureate," in H. Nielsen and K. Nielsen, Ed., *Neighbouring Nobel: The History of Thirteen Danish Nobel Prizes*, Aarhus University Press, Aarhus, 2001, 494-523.
 28. J. J. Pindborg, "The Reparative Effect of Antabuse (Tetraethylthiuram Disulfide) upon Dental Changes in Vitamin E Deficient Rats," *J. Dental Res.*, **1952**, 31, 812-814.
 29. Z. E. Sauna, S. Shukla, and S. V. Ambudkar, "Disulfiram, an Old Drug with New Potential Therapeutic Uses for Human Cancers and Fungal Infections," *Mol. BioSystems*, **2005**, 1, 127-134.
 30. M. Gossop and K. Carroll, "Disulfiram, Cocaine, and Alcohol: Two Outcomes for the Price of One?" *Alcohol & Alcoholism*, **2006**, 41, 119-120.

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AMERICIUM – FROM DISCOVERY TO THE SMOKE DETECTOR AND BEYOND*

Keith Kostecka, Columbia College-Chicago

Introduction

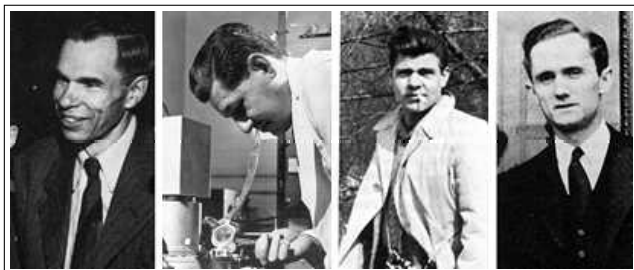


Figure 1. (left to right). Glenn Seaborg, Albert Ghiorso, Ralph James and Tom Morgan.

Since its isolation by Seaborg and his colleagues in 1944, americium has proven to be an element that is quite useful. Discussion of the discovery, announcement of and naming of this element, its characteristics, isotopes, applications [including in smoke detectors], use as a portable gamma ray source, and as a fuel for spacecraft will be described. The chemistry of americium and also work being done to reduce the radio-toxicity of the waste from the reprocessing of used nuclear fuel will also be noted.

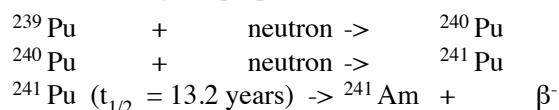
Discovery, Announcement, and Naming

Discovery

In late 1944, in what was the University of Chicago's wartime Metallurgical Laboratory [now Argonne Na-

tional Laboratory], Seaborg, Ghiorso, James, and Morgan (Fig. 1) were the first to “produce” the synthetic element number 95 (1 - 3). This was accomplished through the reaction seen in Figure 2

Figure 2. Seaborg led preparation of Americium-241.



[it is now known that Plutonium-241 has a half-life of 14.4 years (4)]. This discovery was verified by using tracer techniques, given that there were only a few billion atoms available of this new element to study (2). Element 95 was the fourth transuranium element to be discovered, and it was only isolated in amassable quantities in the fall of 1945 (5). It is fascinating to note that the method used to isolate this element warranted a patent in 1964 (6).

Announcement

Given that much of the work of Seaborg and his colleagues during WWII was directly related to the war effort, announcement of important discoveries such as new elements in the periodic table had to be delayed until after the war ended before the work could be de-classified.

This was done informally and unintentionally on live radio on the NBC game show “Quiz Kids” on November 11, 1945 (7). Seaborg, appearing as a guest on the show [which featured children with high IQs and included future (1962) Nobelist James D. Watson], was asked by

Richard Williams whether any new elements, in addition to plutonium and neptunium, had been discovered at Seaborg's laboratory during the war.

This question was very appropriate since the discovery information had been "prepared" for announcement at an American Chemical Society meeting on November 16. Seaborg answered Williams's question by saying that two new elements with atomic numbers of 95 and 96 had been discovered (8).

Naming

Element 95 was included in one more radio appearance before it finally received a name. Seaborg, appearing on the December 15, 1945 airing of the radio program "Adventures in Science," responded to the announcer's question as to whether elements 95 and 96 had been named by stating "...naming one of the fundamental substances of the universe is, of course, something that should only be done after careful thought" (7). The announcer then suggested that listeners should submit their ideas to the program. Those who sent in ideas received a free issue of *Chemistry* magazine that included Seaborg's technical paper and a newly revised periodic table. Ideas received by the program and submitted to Seaborg are shown in Table 1.

Table 1. Selected Proposed Names for Element 95

Big dipperain
Sunonium
Artifium
Artifician
Cyclo
Mechanicium
Curium
Americium

Ultimately, because of the position of element 95 in the periodic table and since its lanthanide homolog, europium, was named after Europe, it made perfect sense to Seaborg that element 95 be named "americium." Thus, it was so named!

Characteristics

Americium, the 95th element in the periodic table, is a synthetic solid metal having a silver and white luster that tarnishes slowly in dry air at room temperature (3). It is fairly malleable and has a relative atomic mass of 243. Selected properties of this element are listed in Table 2 (9 - 12).

Table 2. Selected Characteristics of Americium.

Density	13.69 g/cm ³
Melting point	1449 K
Boiling point	2284 K
Oxidation states	4 (+3, +4, +5 and +6)
Atomic radius	173 pm
Crystal structure	Hexagonal
Molar volume	17.78 cm ³ /mol
Heat of fusion	14.4 kJ/mol
Heat of vaporization	238.5 kJ/mol
Cost, pure	\$160/mg (Am-243)

Isotopes

Eighteen isotopes of the element have been characterized, the most stable [and useful] having masses of 243 and 241. Am-243 has a half-life of 7,370 years but has no broad commercial use. Am-241, termed the "most useful actinide isotope" by Navratil, Schulz, and Seaborg, and now available in kilogram quantities, has a half-life of 432 years (5, 13). It has an alpha activity approximately three times that of radium. When it is handled in gram quantities, it exhibits intense gamma activity but has not been found to cause cancer in humans (14). In addition, although it is fissionable, its critical mass of about 60 kilograms is much higher than that of isotopes of plutonium and uranium; and therefore Am-241 is a poor choice for use in a nuclear device.

Applications

The use (and possible future use) of this element can best be seen in four areas: a neutron source; alpha-ionizing radiation; gamma transmission properties; and as a potential fuel for spacecraft.

Neutron sources containing Am-241 that furnish alpha particles find use in oil well logging, determining soil density and moisture content, measuring moisture content of coke and concrete, and in the activation analysis of a variety of materials as well as for the testing of neutron counters (5, 15). Am-241 is also useful for its alpha-ionizing radiation ability. This is manifested in its applications to determine gas density, serve as an ionization detector in gas chromatography, aid in the preparation of luminous paint, determine the unifor-



Figure 3. Residential ceiling-mounted smoke detector.

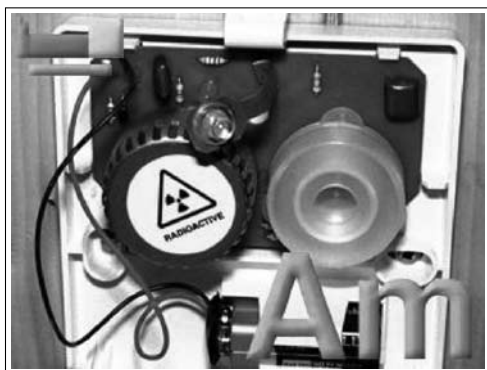


Figure 4. Inside a smoke detector.

mity of thin films, and help to determine the relative humidity of air (5).

Of all the applications of Am-241, however, there is one most familiar to householders everywhere: the smoke detector (Fig. 3 and 4). In a typical smoke detector, americium oxide is bonded to a substrate and exposed directly to the air inside (16, 17). In the sensing chamber the americium oxide ionizes the air so that it becomes a conductor of electricity. Electric current then flows between the two electrodes in the unit; but the electricity flow can be interrupted when tiny smoke particles enter the detector's chamber. If this occurs, the alarm circuit is triggered (5). Anyone having a working smoke detector in the home will have double the chance to survive a fire.

Am-241 has also been used as a portable gamma ray source in radiography. Possible uses are in medicine where gamma emission of Am-241 has allowed the determination of mineral content of bones, lipid content of soft tissues, and body composition (5). Other applications in radiography abound in mineralogy, soil science, and in hydrology (18). Of further interest is the use of this isotope in industrial gauging of materials [for possible internal defects] such as in analysis of metal castings and welded joints (Fig. 5). Imperfections in brake liners and in clutches in manual transmissions can also be detected through this process.

Another use, though with a different isotope, could be as an advanced nuclear rocket propulsion fuel through use of the Am-242m isotope. This work, demonstrated by scientists at Ben-Gurion University of the Negev, may allow trips from Earth to Mars in as little as two weeks (19)! This fairly rare nuclear material could likely maintain nuclear fission existing as an extremely thin metallic film while its high-energy, high-temperature fission fragments escape from the fuel and can thereby lead to faster interplanetary travel.

Chemistry of the Element

The chemistry of this element is best described through its synthesized compounds of Am-241 and in efforts to reduce radiotoxicity of spent nuclear fuel.

Compounds

The first compound of americium [$\text{Am}(\text{OH})_3$] was isolated in the fall of 1945 by Cunningham (5). A variety of halides, oxides, carbonates and sulfates have been prepared and are noted in Table 3 (20). It is apparent that the "preferred" charge for Americium in these compounds is +3.

Table 3. Selected Compounds of Americium

Oxides:	AmO_2 , Am_2O_3 , $\text{AmO}_{1.6-1.9}$
Halides:	AmF_3 , AmF_4 , AmO_2F_2 , AmCl_2 , AmCl_3 , AmOCl , AmBr_3 , AmBr_2 , AmI_2 , AmI_3 , AmOI
Carbonates:	$\text{Am}_2(\text{CO}_3)_3$, MAmOCO_3
Sulfates:	$\text{Am}_2(\text{SO}_4)_3$, $\text{MAm}(\text{SO}_4)_2$

More recent work has led to the preparation and study of nitrides, phosphides, sulfides, monochalcogenides, and monopnictides of americium (21 - 24). This work has included the study of how pressure affects the nature of the element's 5f electrons (25) and even the pressure effects on the superconductivity of AnTGa_5 systems where $\text{An} = \text{Np}$, Pu and Am , while $\text{T} = \text{Co}$, Rh and Ir (26).



Figure 5. Gamma radiography.

Reducing Radio-toxicity

Given that americium and other transplutonium elements are responsible for much of the long-lived radiotoxicity of spent nuclear fuel, a great deal of work has [and is being] done on the extraction of americium (3). If americium and curium are so removed, the remaining spent fuel

would thus require a shorter isolation time. Efforts to address this challenge have involved the use of triazines and other compounds as potential extraction agents (27). The use of 2,6-di(5,6-dipropyl-1,2,4-triazin-3-yl)pyridine was reported to lead to a 99.95% removal of americium from a feed phase, while a synergistic mixture of di(chlorophenyl)dithiophosphinic acid and tri-*n*-octyl phosphine oxide as extractants led to a 99.996% removal (28). Researchers are also identifying molecules such as the Klaui ligand, which has the ability to extract actinides from the environment (Fig. 6). In fact, this compound begs the question: Computational Actinide Chemistry: Are we there yet (29)?

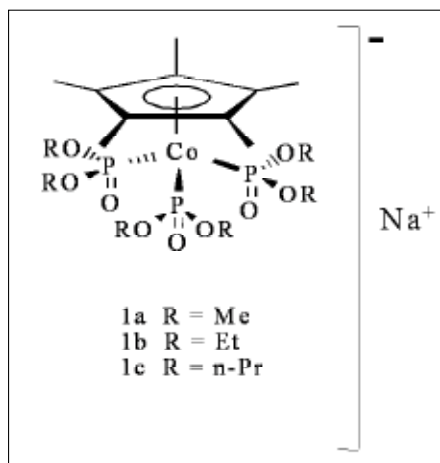


Figure 6. Structure of the Klaui ligand.

Conclusion

It has been clearly shown that americium is an element of significant interest through a consideration of its history from discovery to its applications and beyond.

ACKNOWLEDGMENTS

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REFERENCES AND NOTES

* Presented before the History of Chemistry Division at the 234th American Chemical Society Meeting, Boston, MA, August 19, 2007, HIST 001.

- G. T. Seaborg and J. J. Katz, *The Transuranium Elements*, NNES-IV-14B, McGraw-Hill Book Co., New York, 1949.
- T. K. Keenan. "Americium and Curium," *J. Chem. Educ.*, **1959**, 36, 27-31.
- Americium; <http://en.wikipedia.org/wiki/Americium> (accessed May, 2008).

- Science for the Critical Masses: How Plutonium Changes with Time. Available at <http://www.ieer.org/ensec/no-3/puchange.html> (accessed May, 2008).
- J. D. Navratil, W. W. Schulz, and G. T. Seaborg. "The Most Useful Actinide Isotope: Americium-241," *J. Chem. Educ.*, **1990**, 67, 15-16.
- Patent number 3,156,523, "Element 95 and Method of Producing Said Element." Available through <http://patft.uspto.gov/netahtml/PTO/srchnum.htm> (accessed May, 2008).
- Americium: <http://pubs.acs.org/cen/80th/print/americi-unprint.html> (accessed May, 2008).
- The author has yet to discover exactly what ACS meeting was meant here. There were no national ACS meetings during 1945.
- It's Elemental – Americium: <http://education.jlab.org/itselemental/ele095.html> (accessed May, 2008).
- Americium: <http://www.periodni.com/en/am.html> (accessed May, 2008).
- Americium: <http://periodic.lanl.gov/elements/95.html> (accessed May, 2008).
- Spectrum, Chemical Fact Sheet – Americium: <http://www.speclab.com/elements/americium.htm> (accessed May, 2008).
- When Am-241 was first put up for sale in 1962 by the US Atomic Energy Commission, it cost \$1,500/gram.
- ToxFAQs for Americium: <http://www.atsdr.cdc.gov/tfacts156.html> (accessed May, 2008).
- Moisture and Density "Nuclear" Gauges Used in Road Construction: <http://www.epa.gov/radtown/gauges.html> (accessed May, 2008).
- Health Physics Society: <http://www.hps.org/publicinformation/ate/q4738.html> (accessed May, 2008).
- In fact, one gram of americium oxide provides enough active material for about 5,000 smoke detectors. This compound, in addition, gives a radiation dose to homeowners of essentially zero.
- A Gamma-Ray Source for Use In Radiography: <http://www.freepatentsonline.com/EP1200966.html> (accessed May, 2008).
- Extremely Efficient Nuclear Fuel Could Take Man To Mars In Just Two Weeks: <http://www.sciencedaily.com/releases/2001/01/010103073253.htm> (accessed May, 2008).
- F. A. Cotton and G. Wilkinson, *Advanced Inorganic Chemistry – A Comprehensive Text*, John Wiley and Sons, New York, 1980.
- Synthesis of actinide nitrides, phosphides, sulfides and oxides: <http://www.freepatentsonline.com/5128112.html> (accessed May, 2008).
- L. Petit, A. Svane, W. M. Temmerman, and Z. Szotek. "Valency in Actinides," *Solid State Commun.*, **2000**, 116, 379-383.
- L. Petit, A. Svane, W. M. Temmerman, and Z. Szotek, "Self-interaction Corrected Description of the Elec-

- tronic Properties of Americium Monochalcogenides and Monopnictides, *Phys. Rev. B*, **2001**, 63, 165107.
24. L. Petit, A. Svane, W. M. Temmerman, and Z. Szotek. "Electronic structure of Pu Monochalcogenides and Monopnictides," *Eur. Phys. J. B*, **2002**, 25, 139-146.
25. S. Heathman, R.G. Haire, T. Le Bihan, A. Lindbaum, K. Liftin, Y. Meresse, and H. Libotte. "Pressure Induces Major Changes in the Nature of Americium's 5f Electrons," *Phys. Rev. Lett.*, **2000**, 85, 2961-2964.
26. Pressure Effect on the Superconductivity of AnTGa Systems and Americium metal (An = Np, Pu, Am – T = Co, Rh, Ir): http://www.mrs.org/s_mrs/sec_subscribe.asp?CID=6210&DID=170299&action=detail (accessed May, 2008).
27. M. J. Hudson, M. G. B. Drew, M. R. St. J., Foreman, C. Hill, N. Huet, C. Madic, and T.G.A. Youngs. "The Coordination Chemistry of 1,2,4-Triazinylbipyridines with Lanthanide (III) Elements – Implications for the Portioning of Americium (III)," *J. Chem. Soc. Dalton Trans.*, **2003**, 1675-1685.
28. A. Geist, M. Weigl, and K. Gompper. "Effective Actinide (III)-Lanthanide (III) Separation in Miniature Hollow Fibre Modules. 7th Information Exchange Meeting on Actinide and Fission Product Partitioning and Transmutation, 2002. OECD Nuclear Agency. Available at <http://www.nea.fr/html/pt/docs/iem/jeju02/session2/SessionII-15.pdf> (accessed May, 2008).
29. Computational Actinide Chemistry: Are we there yet? http://www.eurekaalert.org/pub_releases/2007-08/dnnl-cac081307.php (accessed May, 2008).

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FUTURE ACS MEETINGS

March 22-26, **2009**—Salt Lake City, UT
August 16-20, **2009**—Washington, DC
March 21-25, **2010**—San Francisco, CA
August 22-26, **2010**—Boston, MA
March 27-31, **2011**—Anaheim, CA
August 28-September 1, **2011**—Chicago, IL
March 25-29, **2012**—San Diego, CA
August 19-23, **2012**—New York, NY
April 7-11, **2013**—New Orleans, LA
September 8-12, **2013**—Indianapolis, IN
March 16-20, **2014**—Washington, DC
September 7-11, **2014**—San Francisco, CA
March 22-26, **2015**—Denver, CO
August 16-10, **2015**—Boston, MA
March 13-17, **2016**—San Diego, CA
August 21-25, **2016**—Philadelphia, PA
April 2-6, **2017**, San Francisco
September 10-14, **2017**, St. Louis

THE GORDON RESEARCH CONFERENCES AS SCIENTIFIC INFRASTRUCTURE

Arthur Daemmrich, Harvard Business School, and Leah Shaper, Freelance Science Writer

Introduction

Conferences serve as a crucial part of scientific infrastructure by offering participants the opportunity to announce novel findings, discuss research methods, and take part in a variety of networking activities. Presenting papers and learning about unpublished new work are vital for scientists to stay current in their discipline. Yet conferences have drawn minimal attention from historians and sociologists of science, whose analysis of scientific infrastructure has instead focused on formal scientific communication through journal articles and on-line forums, the formation of new disciplines and subfields, and shifting funding structures for academic and industrial laboratories (1).

This article focuses on the Gordon Research Conferences (GRC) as a historically unique conference format and management structure. Unlike general professional or society meetings that typically feature short talks, multiple parallel sessions, and efforts to attract media coverage, Gordon Conferences are topically specific, have extensive discussion periods but few formal talks, and are closed to the press. From their modest origins in summer sessions held at Johns Hopkins University in the late 1920s and early 1930s, the Gordon Conferences have grown into meetings that cover over 350 topics and attract more than 20,000 participants annually. We argue that GRC's growth is a product of internal and external factors: conferences stimulate intensive discussion and real-time peer review; new topics are chosen through a

review process oriented to frontier areas of science; and the GRC format fosters intimacy among participants even as the overall size of the scientific enterprise expands. This article explores how the GRC organization managed growth over time and maintained a sense of community within the conferences. More generally, we seek to make visible the inconspicuous roles of fostering the exchange of new ideas, helping form collaborations, advancing institutional changes, and promoting the development of commercial products that conferences play within the scientific community. The article concludes with a description of current challenges faced by GRC and other conference organizers.

GRC's Foundations

The chemistry department at Johns Hopkins University (JHU) began hosting an intermittent set of summer meetings in the late 1920s. Under the leadership of Ira Remsen, JHU had by then already pioneered research-based chemical education in the United States. Its chemistry department was training students for positions in both academia and growing industrial research laboratories (2). Beginning in 1931, summer sessions were held each year to present new findings in chemistry and chemical instrumentation. Graduate students could take the sessions for credit, and prominent academics from across the country appealed to chemistry professor Donald H. Andrews and later to Neil Elbridge Gordon for permission to attend.

Early in his life, Gordon displayed affinities for both chemistry and meeting organization. While in high school in upstate New York he arranged an after-school science club at which “papers provoked animated discussion which continued long past the time for adjournment” (3). Following study at Syracuse University in mathematics and chemistry, Gordon earned a Ph.D. in chemistry from JHU in 1917. By 1928 he was back at JHU as the Garvan Chair of Chemical Education. In the interim he had begun to influence the field, including prompting the American Chemical Society to create the Section (since 1924, “Division”) of Chemical Education in 1921, launching the *Journal of Chemical Education* in 1924, and publishing a textbook, *Introductory Chemistry*, in 1927 (4). As Garvan Chair, Gordon took the lead in organizing the JHU conferences; he narrowed their focus to one topic per session and broadened participation to include scientists from industry and government laboratories. Topics for the week-long conferences in the early years included the Raman effect and molecular structure, colloidal chemistry, catalysis, x-ray crystallography, and organic chemistry (5).

Seeking a more remote location, Gordon relocated the series in 1934 to Gibson Island, Maryland, located some 30 miles from Baltimore on the Chesapeake Bay (6). The research conferences met at the Gibson Island Club during the summers of 1934, 1935, and 1936. Advertised as a way to learn about “frontier problems” in topics ranging from analytical chemistry to nuclear physics, the conferences reflected Gordon’s belief that scientific innovation was fostered by formal presentations in conjunction with informal discussion. He was unhappy with the size of most other scientific conferences of the time. Each of his conferences, he stated, had to have a

chairman of noted authority in his field, leaders to focus discussion on current advances of scientific work, and groups limited in size to encourage dynamic discourse (7). Researchers were drawn by the topics, the location, and by Gordon’s ability to stimulate open communication among scientists from academia, industry, and government research institutions.

GRC in Transition

Through the late 1930s and early 1940s, participation in the conferences continued to grow, and conferees’ topical interests became more clearly focused. A set of core conference series had taken shape by 1945; many of these meetings, or their current incarnations, are still held today. Even as topics evolved through the 1930s and early 1940s, Gordon worked to ensure the conferences’ stability. As secretary of the American Association for the Advancement of Science (AAAS) Section C (Chemistry), Gordon persuaded AAAS to take on a formal role in managing the conferences. AAAS agreed to make the conferences a participating organization, on the condition that they would remain financially independent (8). Gordon served as secretary for the conferences in 1938 and 1939 and was officially appointed their director in fall 1939.

The number of conferences grew quickly from two in 1938 to eight in 1941. Seeking to expand beyond the limited facilities of the Gibson Island Club, Gordon secured funds from AAAS and some thirty-three corporations to purchase a property on the island, known as the Symington House. Conferences were held on the house porch as well as at the Gibson Island Club. For many years, these founding companies and follow-on industrial sponsors were guaranteed registration slots for qualified

Table 1. Name Lineage of Gordon Research Conferences

1931-1932	Summer Session of the Chemistry Department at Johns Hopkins University
1933	Conference on Recent Developments in Chemistry at Johns Hopkins University
1934	Research Conferences on Chemical Physics
1935	Johns Hopkins University Research Conferences on Chemical Problems
1936	Johns Hopkins University Research Conferences in Biology, Chemistry, and Physics
1937	Seventh Annual Research Conference of the Department of Chemistry of the Johns Hopkins University
1938 - 1941	Special Research Conferences on Chemistry
1942 - 1946	AAAS–Gibson Island Research Conferences
1947	Chemical Research Conferences
1948 - present	Gordon Research Conferences

scientists from their research laboratories. In 1942 the conferences came to be called the *AAAS-Gibson Island Research Conferences* (see Table 1 for the GRC name lineage).

The link to AAAS helped ensure continuity for the conferences during changes in leadership and governance structure in the mid-1940s. Gordon accepted an offer to chair Wayne State University's chemistry department in 1942 and in 1945 turned over most of his conference responsibilities to a colleague, polymer chemist Sumner B. Twiss. Both Gordon and Twiss resigned in 1946, and members of the conferences' management committee, chaired by George Calingaert from Ethyl Corporation, began searching for a new director.

The committee also faced tensions with Gibson Island residents regarding conference growth and the participation of African American scientists. In a notorious incident, Percy Julian initially was not permitted to enter the Gibson Island Club to participate in the 1943 hormone conference. He reportedly was only able to join the meeting "after three days of protesting by members of the conference" (9). Among the protestors was Gregory Pincus, who subsequently chaired a meeting on hormone research at Mont Tremblant, Quebec, which grew into the annual Laurentian Hormone Conference series (10). Other complaints in the mid-1940s included inadequate sleeping facilities, poor housekeeping, insufficient meeting rooms, and bad food. Overall, as Sumner Twiss reported to George Calingaert in August 1946, "On the Island there is an Aristocracy of Wealth ... the conferences are an Aristocracy of Brains" (11). Even though Twiss suggested ways for each side to better appreciate the other, the management committee began to look at other locations.

Among possible sites the committee visited Dartmouth College, and on its way back to Boston chanced upon Colby Junior College (renamed Colby-Sawyer College in 1975) in New London, New Hampshire. They found Colby's cool temperatures, classrooms, and dorms a pleasant contrast to Gibson Island. After an impromptu meeting with its president, H. Leslie Sawyer, the college was chosen as the new site in 1947 (12). Shortly thereafter, the management committee elected W. George Parks as the new director. That year, ten *Chemical Research Conferences* were held at Colby. Before the end of the year, Calingaert had obtained Gordon's permission to adopt the name *Gordon Research Conferences*, which was made official at an April, 1948 dedication ceremony (13). Tragically, Gordon was unable to witness the sub-

sequent growth of the conferences. After a long-standing battle with his physical and mental health, he ended his life in 1949 (14).

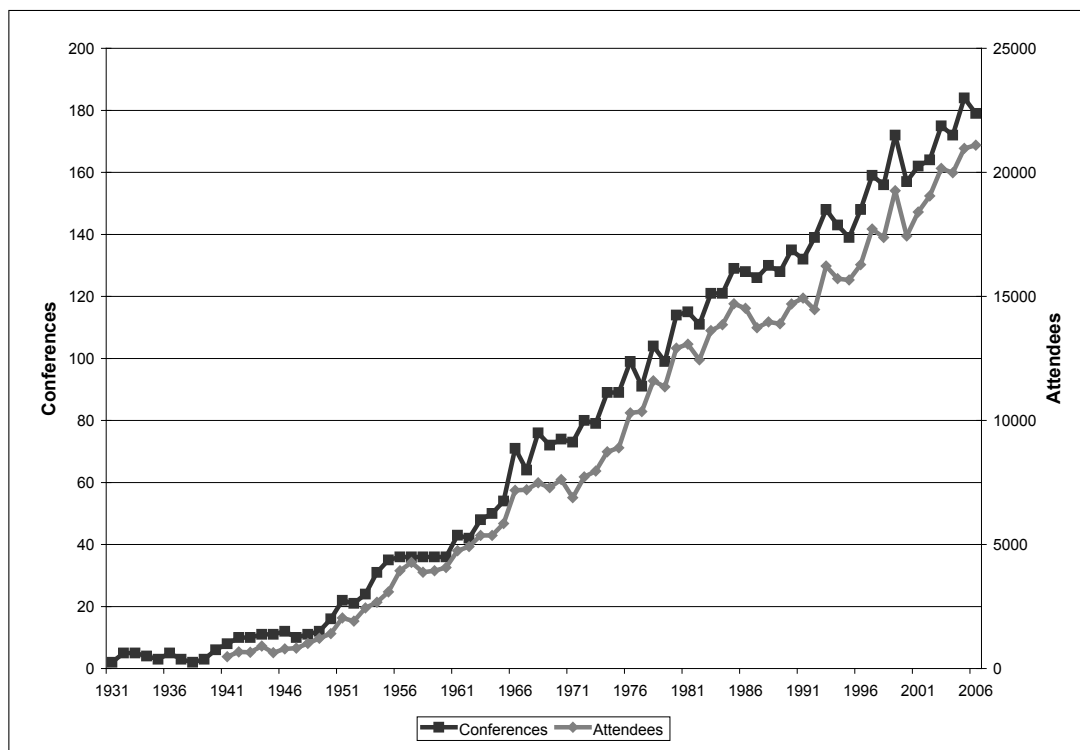
Parks moved conference headquarters to Rhode Island State College (renamed University of Rhode Island in 1951), where he became chairman of the chemistry department in 1950. There he enlisted Alexander M. Cruickshank, a young chemistry instructor and former student, to help manage the conferences, and Alexander's wife Irene Cruickshank to serve as secretary and treasurer. Parks oversaw steady growth in the number of the conferences, attendance, and locations. A survey circulated in 1949 to some five hundred scientists had revealed a strong interest in new topics (15). By its 25th anniversary year in 1956, GRC had grown to thirty-six conferences with nearly four thousand participants from forty-six countries.

Along with expansion came further changes in governance. In 1956 GRC incorporated as a nonprofit organization. A selection and scheduling (S&S) committee was established in 1958 to advise the board on the addition and termination of conferences. Meeting sites continued to grow in number and geography during the 1950s and early 1960s, with conferences held in California starting in 1963. Parks' directorship, however, came to an abrupt end in 1968 in the wake of an IRS investigation into his personal finances. Even though the GRC organization was not implicated in the charges, Parks resigned with encouragement by the GRC board (16).

Continuing Growth and International Expansion

A period of extraordinary growth began in 1968 (see Fig. 1) when Alexander M. Cruickshank was named director, with additional conference sites in New England, meetings in California, and, starting in 1990, Gordon Conferences in Europe. The institution of a less centralized financial structure encouraged conference chairs to apply for federal grants and other support through GRC headquarters. This allowed individual conference series to subsidize the attendance of speakers, graduate students, and other special visitors. Cruickshank worked to maintain accessibility to the conferences by keeping attendance fees low and encouraging an informal and personal atmosphere.

International expansion begun by Cruickshank continued under the leadership of GRC's fourth director, Carlyle B. Storm, with the further addition of sites

Figure 1. Number of Gordon Conferences and Attendees, 1931-2006

in Europe and new conference locations in Asia. Storm retained the unique GRC format, promoted the “GRC brand” conference style focused on discussion, and preserved the place of leading scientists in conference management. Evidence of the organization’s growth and independence came in 2002, when GRC moved from the University of Rhode Island to its own headquarters building. Expansion of GRC meetings and attendees continues under the current director, Nancy Ryan Gray. (See Table 2 for a history of GRC leadership.) In 2006 GRC attracted more than 20,000 participants to conferences at 23 sites in the United States and seven sites overseas.

Conference Operations

GRC’s remarkable growth and success result from a distinctive operating structure that has remained virtually unchanged since the early 1930s, despite transformations in many areas of science and technology. The principles of this format, enumerated in a 1950 publication by the AAAS, still ring true for current GRC attendees: limited numbers of conferees encourage full participation in discussion, the formation of friendships, and impromptu discussions; conferences include a balance of participants from academia, industry, government, and other research institutions; meetings nurture the free exchange of scien-

tific ideas; and documentation or publication of conference discussions or presentations is restricted (17).

The Gordon Conference operating formula puts small groups of scientists into isolated locations for five days with ample discussion time. This structure stimulates advances in fundamental scientific knowledge, generates new experimental techniques, promotes collaborations, shapes science’s institutional structure, and influences the development of products ranging from new polymers to medicines. Table 3 lists a selected set of these outcomes from a survey conducted in 2004 (18).

Remote conference locations provide an environment largely free from other distractions. The 1933 program for conferences at JHU recommended cottages on the Chesapeake Bay from which conference attendees could commute to Baltimore (19). Gordon chose Gibson Island as the new conference site in 1934 for its isolation and vacation-oriented atmosphere. Located near six mountains and several lakes, Colby Junior College provided conferees with cooler temperatures, seclusion, and a variety of recreational opportunities. Conference locations added since that time in New England, California, Europe, and Asia were selected with similar ideals in mind.

Table 2. GRC Directors

Neil E. Gordon	1931 - 1936; 1939 - 1946
W. George Parks	1947 - 1968
Alexander M. Cruickshank	1968 - 1993
Carlyle B. Storm	1993 - 2003
Nancy Ryan Gray	2003 - present

The earliest conferences held at JHU were organized as summer courses taught by chemistry department faculty and visiting specialists over a period of five weeks. One course met each week for five days (Monday to Friday). After the move to Gibson Island, one or two formal lectures were held each day—usually in the morning—followed by discussion periods. The daily schedule and format used today was established in the 1940s: breakfast, formal presentations in the morning, discussions until lunch, afternoons devoted exclusively to free-time, and further talks and discussion in the evening after dinner, with all meals held communally. Especially noteworthy is that afternoons and late evenings are intended for sports, other recreation, and informal discussions. Conferences now run from Sunday night through Friday morning and typically also include time for late-afternoon or evening poster sessions. This atmosphere has established a kind of “real-time” peer review, balanced by afternoon and evening activities that foster collegiality.

As early as 1937, GRC formally announced a policy in its program that restricted the recording or public reference of information presented during a conference (20). GRC does not publish proceedings or permit references to the conferences in published scientific articles; however, it does encourage attendees to publish new findings (often stimulated by discussions at a Gordon Conference) under their own names. This “off-the-record” policy gives conferees the freedom to present and receive critical feedback on novel ideas, fledgling theories, and early experimental results. Poster sessions offer an interesting variation to this policy. Though they might seem to contradict the off-the-record policy, they have been permitted by GRC leadership since being initiated at the 1985 Atomic Physics conference, largely because they stimulate exactly the type of one-to-one and group discussions that GRC aims to achieve (21).

Attendees and Diversity

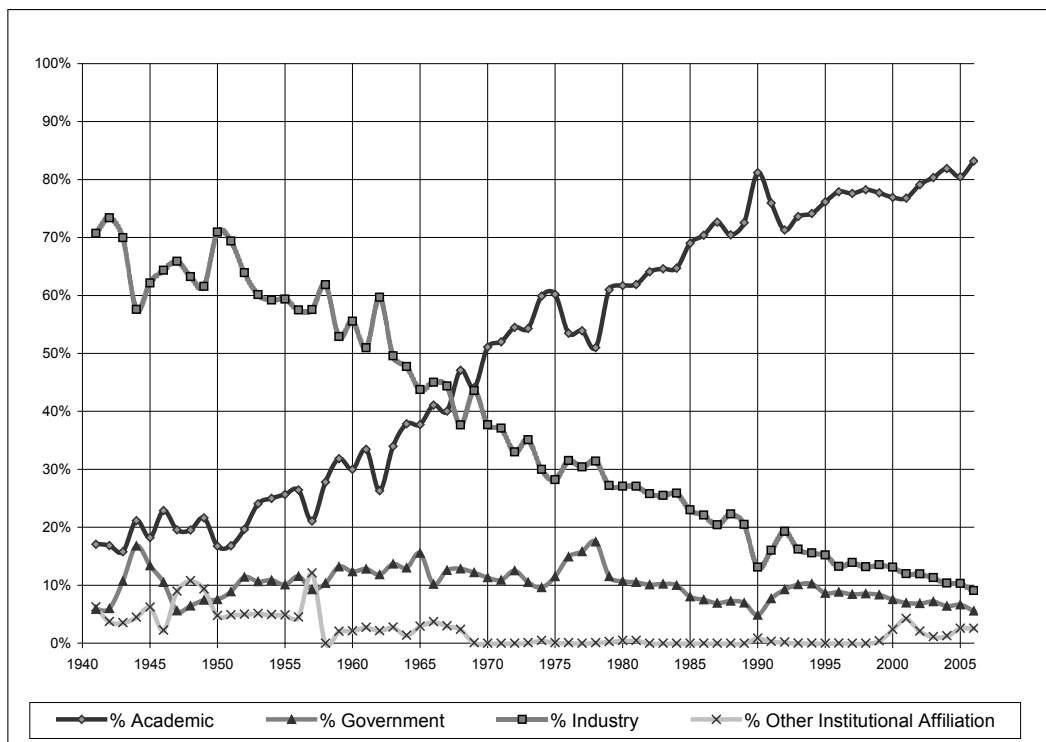
Throughout its history, GRC has sought to keep attendee

numbers small enough to promote full participation and high-quality discussion, but large enough to represent a diversity of perspectives and research approaches. Limited Gibson Island facilities restricted attendance to 60 people per conference in the 1930s and early 1940s. Capacity was increased by the move to New Hampshire in 1947, and board discussions in the 1950s and 1960s set the ideal attendance at 100. Conference registration numbers have increased since then, although meeting room and lodging capacity limit attendance to 135 at many sites. In 2006 conference attendance ranged from 65 to 174, with an overall average of 120 (22).

The balance of academic, industrial, and government scientists at conferences has shifted significantly during GRC’s history. In the 1940s and 1950s, industrial scientists dominated conference attendance. Noting the imbalance, the AAAS committee managing the conferences developed an assistance fund in 1950 to support attendance by scientists from academia and government. Mirroring the post-Sputnik expansion in federal support for academic and government laboratories, academic attendance at GRC began a sharp climb in the late 1950s. By 1969, equal numbers of academic and industrial scientists were in attendance. Since then, the percentage of academic attendance has continued to rise for a number of reasons, including time available to attend a week-long conference and changes in the structure and focus of industrial research. Conference participation today hovers around 81 % academic, just over 10 % from industry, less than 7 % from government, and about 2 % from foundations, nongovernmental organizations, and other institutions.

The percentage of women attending GRC has also increased over time. Already in the 1940s, a handful of female scientists participated in the GRC, particularly in conferences oriented toward the biological sciences. The participation of women remained below 5 % until 1970 but has since increased to nearly 30 % in 2006. GRC’s leadership and governance reflect the organization’s goal of fostering gender equality, with a female director and seven women out of the thirteen-member board of trustees.

A mixture of scientists in various career stages adds new perspectives to conference discussions, facilitates mentoring of younger scientists, and creates a forum for “young Turks” to challenge orthodoxy. GRC has encouraged the participation of graduate students and postdoctoral fellows during the past decade, in part through the Gordon-Kenan Summer School programs.

Figure 2. Institutional Affiliation of Gordon Conference Attendees, 1940-2006

For many young scientists, attending a GRC is the first opportunity to speak in person with world-renowned leaders in their disciplines.

Conclusion

This article has examined GRC in order to draw attention more generally to scientific conferences, an often overlooked element in the institutional structure of science. As the sociologist of science Harry Collins recently argued (23):

...conferences are vital ... little groups talk animatedly about their current work and potential contributions. Face-to-face communication is extraordinarily efficient.

Such animated discussion and high-bandwidth exchange do not happen by coincidence. By analyzing the history and structure of the Gordon Research Conferences as a case study, we have shown how well-designed scientific conferences achieve their educational and community-building goals.

Historians and sociologists of science have long examined the role of communal norms in science and its interface with the public. Yet the important forum that conferences provide to address communal issues ranging from verification of new findings to major disputes has

been largely ignored by social scientists. Scientific meetings like the Gordon Research Conferences, even when intentionally focused on pure research, play a crucial role in the scientific infrastructure and in the process by which new communities are formed. By stimulating frank and critical discussion, they also build consensus on new theories, methods, and results that have impacts well beyond the scientific community.

A significant future challenge for GRC, as well as for other organizations that host scientific conferences, is the overall expansion in meetings. During just the past decade meetings organized by GRC, Keystone Symposia, Cold Spring Harbor Laboratory, the Jackson Laboratory in Maine, and other nonmembership organizations have experienced similar growth curves (24). With the scientific enterprise continuing to increase, especially in Asia, conference organizers operate in an expanding economy. At the same time, the number of meetings that leaders in a specific field can attend is limited, thereby also limiting participation by less established scientists. The competition for top speakers will therefore only intensify in coming years.

Finally, all conferences face the continued challenge of determining what counts as frontier science. Derek Price famously postulated in 1963 that eighty to ninety percent of all scientists who had ever lived were alive

at that moment (25). With scientific growth continuing at an exponential rate, that percentage has increased in the interim. Yet GRC and other organizations run a finite number of conferences for a comparably modest number of attendees. The mechanisms used by GRC for setting conference programs and evaluating content described here have been very successful. A key question for the future is whether GRC's governance tools, including the S&S committee and internal selection of conference chairs, can keep pace with the ever growing number of conferences. Are these mechanisms infinitely scalable, or are they eventually size-dependent? The model thus far has relied on modestly sized conferences in remote locations, which strongly suggests an upper limit to the size of any one conference. The total number of intimate conferences that one organization can effectively manage, however, is likely quite large so long as review mechanisms ensure high quality presentations and discussion.

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REFERENCES AND NOTES

1. E. J. Hackett, O. Amsterdamska, M. Lynch, and J. Wajman, *The Handbook of Science and Technology Studies*, MIT Press, Cambridge, MA, 3rd ed., 2007; J. Ben-David, *Scientific Growth: Essays on the Social Organization and Ethos of Science*, University of California Press, Berkeley, CA, 1991.
2. L. Reich, *The Making of American Industrial Research: Science and Business at GE and Bell, 1876-1926*, Cambridge University Press, New York, 1988; D. Hounshell and J. K. Smith, *Science and Corporate Strategy: DuPont R&D, 1902-1980*, Cambridge University Press, New York, 1988.
3. N. E. Gordon, "The Value of a Science Club in Secondary Schools," *School Science and Mathematics*, 1917, 17, 802-804.
4. N. E. Gordon, *Introductory Chemistry*, World Book Company, New York, 1927.
5. D. H. Andrews, "The Summer Session of the Chemistry Department of the Johns Hopkins University," *Science*, **1932**, 75, 303-304; N. E. Gordon, "Conference on Recent Developments in Chemistry at the Johns Hopkins University," *Science*, **1933**, 77, 320-321.
6. E. Ott, "Significance of the Gordon Research Conferences," *Science*, **1954**, 119, 487-489.
7. N. E. Gordon, "Research Conferences on Chemical Physics," *Science*, **1934**, 79, 176-177; N. E. Gordon, "The Johns Hopkins University Research Conferences on Chemical Problems," *Science*, **1935**, 81, 310-311; N. E. Gordon, "The Johns Hopkins University Research Conferences in Biology, Chemistry, and Physics," *Science*, **1936**, 83, 386.
8. W. G. Parks, "Gordon Research Conferences: A Quarter-Century on the Frontiers of Science," *Science*, **1956**, 124, 1279-1281.
9. D. Ingle, "Gregory Goodwin Pincus," in *Biogr. Mem. Natl. Acad. Sci. USA*, Columbia University Press, New York, Vol. 42, 1971, 233.
10. G. Pincus, "The Hormone Conference in Quebec," *Science*, **1944**, 99, 143.
11. Letter from S. Twiss to G. Calingaert, August 13, 1946. A copy of this letter and references to racial issues on the island involving Percy Julian were generously provided by an anonymous reviewer.
12. A. M. Cruickshank, interviewed by Arthur Daemmrich at New London, NH, August 19, 2002, Chemical Heritage Foundation, Philadelphia, PA, Oral History Collection.
13. Records of the Gordon Research Conferences, Chemical Heritage Foundation, correspondence between Calingaert and Gordon, October 1947, box 2/6; Faculty Bulletin of Wayne University, April 21, 1948, box 1/8.
14. R. B. Hahn, "The Early Days of the Chemistry Department at Wayne State University," published on-line: <http://www.chem.wayne.edu/information/history.html> (accessed May 2007); F. Gordon, *The Price of Decision: Neil Elbridge Gordon, 1886-1949*, University of Louisville, Louisville, KY, 1985, 313-314.
15. Records of the Gordon Research Conferences, Chemical Heritage Foundation, "The Gordon Research Conferences," internal memorandum of the American Association for the Advancement of Science (1950), box 5/3.
16. R.W. Parry, interviewed by Arthur Daemmrich and Arnold Thackray at Salt Lake City, UT, July 19, 2002, Chemical Heritage Foundation, Philadelphia, Oral History Collection.
17. Records of the Gordon Research Conferences, Chemical Heritage Foundation. "The Gordon Research Conferences," AAAS (1950), box 5/3.
18. "Outcomes of the Gordon Research Conferences." Survey mailed to 4,000 past attendees of Gordon Research Conferences in spring 2004; total return of 593 (14.8%). Archived with Records of the Gordon Research Conferences, Chemical Heritage Foundation.

19. N. E. Gordon, "Conference on Recent Developments in Chemistry at the Johns Hopkins University," *Science*, **1933**, 77, 320-321.
20. F. O. Rice, "Scientific News and Notes," *Science*, **1937**, 85, 580.
21. Harold Metcalf, survey response, Outcomes of the Gordon Research Conferences, Spring 2004.
22. Internal operations database, Gordon Research Conferences, West Kingston, RI.
23. H. M. Collins, *Gravity's Shadow: The Search for Gravitational Waves*, University of Chicago Press, Chicago, IL, 2004, 450-451.
24. K. O'Brien, "The Future of Scientific Meetings," *The Scientist*, May, 2006, 50-56.
25. D. Price, *Little Science, Big Science*, Columbia University Press, New York, 1963, 1-2.

Table 3. Selected Outcomes of the Gordon Research Conferences

Outcome Type	Result
Theoretical Knowledge	<ul style="list-style-type: none"> • The mechanism and structure of ATP synthase was reported by both Paul Boyer and John Walker at the 1981 Bioenergetics conference. • Understanding of atomic laser cooling and Bose-Einstein condensation evolved at Atomic Physics conferences in the 1980s and early 1990s. Six physicists who attended these conferences were awarded Nobel laureates for these achievements.
Experimental Techniques	<ul style="list-style-type: none"> • Polarization experiments, electrochemical impedance spectra, and the use of current potential measurements developed at the Corrosion conferences in the 1950s and 1960s fostered understanding of the dynamics of corrosion. • Successful recombinant DNA (rDNA) techniques developed by Herbert Boyer and Stanley Cohen were described at the 1973 Nucleic Acids conference; co-chairs Maxine Singer and Dieter Söll then set aside extra time for attendees to discuss the broader implications of this breakthrough.
Collaborations	<ul style="list-style-type: none"> • The discovery of the 5' terminal cap structure in cellular and viral messenger RNAs was facilitated by the exchange of experimental findings among Robert P. Perry, Bernard Moss, Fritz Rottman, and Aaron Shatkin at the 1974 Animal Cells and Viruses conference. • Jointly published papers on frustrated smectic liquid crystals and liquid crystal phase transitions were the result of a collaboration formed between Carl W. Garland and Ranganathan Shashidhar at the Liquid Crystal conferences.
Institutional Changes	<ul style="list-style-type: none"> • The Society of Toxicology was formed in 1961 as a direct result of the Mechanisms of Toxicity conference. This conference was also key to the development of the Environmental Mutagen Society in 1969. • The International Society for the Study of Xenobiotics (ISSX), an international drug metabolism society, was formed in 1981 by Bruce Migdalof and a small group of participants in the 1980 Drug Metabolism conference.
Commercial Products	<ul style="list-style-type: none"> • A better understanding of the properties and synthesis of polymers and such nonmelting thermally stable fibers as Nomex and Kevlar came out of the Polymer conferences, which have been meeting since the 1930s. • The application of eflornithine as the first new drug treatment for African sleeping sickness in over 40 years was developed by Cyrus J. Bacchi after he obtained a sample from Peter McCann at the 1979 Polyamines conference.

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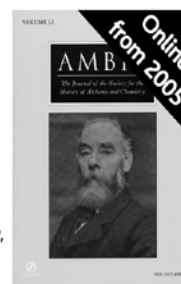
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A HISTORY OF CARBOHYDRATE RESEARCH AT THE USDA LABORATORY IN PEORIA, ILLINOIS*

Gregory L. Côté and Victoria L. Finkenstadt, U.S. Department of Agriculture

Origins

The history of the United States Department of Agriculture (USDA) can be traced back to the Agricultural Division of the US Patent Office (1), so it is perhaps not unexpected that the USDA is still active in the development and patenting of many useful inventions related to agriculture. The Utilization Laboratories of the USDA have been especially involved in this type of activity. This article focuses on the National Center for Agricultural Utilization Research (NCAUR), located in Peoria, Illinois, and its important historical contributions in the field of carbohydrate research.

During the years of the Great Depression, the American farm economy was in dire straits. Prices were low, and farmers were going bankrupt at unprecedented rates. There was a great public outcry for the federal government to do something about the situation, but price supports and other similar programs were not seen as a long-term solution. One obvious solution was to create new markets for farm goods, but this required a long-term investment in research and development. However, there was little infrastructure in place to carry out this type of work. Attention began to turn to those who had been active in this type of research, as exemplified by George Washington Carver, among others. These researchers were at the forefront of a movement that became known as “chemurgy,” which focused on the conversion of natural commodities to new and useful materials (2). This techno-political movement resulted in the forma-

tion of the National Farm Chemurgic Council (NFCC) in the mid-1930s. Led by such well-known figures as Henry Ford, a proponent of products like corn-derived ethanol fuels and soybean-based plastics, the movement eventually resulted in action by the federal government. Section 202 of the Agricultural Adjustment Act of 1938 states in part:

The secretary (of Agriculture) is hereby authorized and directed to establish, equip, and maintain four regional research laboratories, one in each major farm producing area, and at such laboratories conduct researches into and to develop new scientific, chemical and technical uses and new and extended markets and outlets for farm commodities and products and byproducts thereof. Such research and development shall be devoted primarily to those farm commodities in which there are regular or seasonal surpluses, and their products and byproducts.

The Regional Research Laboratories, built at the initial cost of approximately one million dollars each, were established in Wyndmoor, PA (Eastern); Peoria, IL (Northern, now NCAUR); New Orleans, LA (Southern); and Albany, CA (Western). A fifth facility was established during the 1960s in Athens, GA (Southeastern). Each of the original four was initially assigned the task of creating new products from crops grown in their respective region, but it eventually proved difficult to delineate scientific research on such a basis. All four of the original laboratories have distinguished themselves by a proud history of research and development, and their accomplishments

have been summarized in a number of publications (3). The four original Regional Research Laboratories have been designated National or International Chemical Historic Landmarks (4). In 1953 the USDA formally created the Agricultural Research Service (ARS) to be its chief in-house science agency. In the 54 years since then, ARS has been a significant contributor to agricultural progress and earned a global reputation as a scientific organization whose research has benefited the farmer, the consumer, and the environment.



A contemporary postcard view of the Northern Regional Research Laboratory as it appeared in the 1940s.

Early Research: The 1940s and '50s

The Northern Regional Research Laboratory (NRRL) was assigned the job of finding new uses for corn, wheat, and agricultural waste materials. Soybeans were not included because soy was not considered a major cash crop at that time. NRRL research in oil chemistry would play a role in changing that. Fittingly, an ear of corn encased in a block of the then-new acrylic resin was included in the items placed in the cornerstone of the building, for corn was and is still a cornerstone of the Midwest economy and NRRL research efforts. From the day its doors opened in December of 1940, it was clear that a major portion of the research carried out at NRRL would focus on carbohydrates, since a major constituent of the locally grown wheat and corn is the complex carbohydrate known as starch. Cornstarch was already being converted to corn syrup, used as a sweetener and fermentation medium for alcohol production. In order to investigate ways to improve and better understand the process, a Starch and Dextrose Division was set up at NRRL. A Fermentation Division was also established, for similar reasons. The Fermentation Division would soon become famous for its wartime role in the development of penicillin (5), and the milk sugar lactose played

a part in that story (6). It would be the first of many carbohydrate-related contributions by NRRL scientists.

When research first began at NRRL, one of the goals was to improve the conversion of starch to glucose so that it could be converted to fuel alcohol (ethanol) more cheaply and efficiently. At that time, ethanol for fuels and industrial solvents was more efficiently produced from sugar molasses than from grain. However, German U-boat attacks on shipping in the Caribbean seriously threatened the source of molasses. As Peoria was historically a hub for the grain alcohol distilling industry, it is not surprising that researchers would find it a fruitful place to work on alternatives for alcohol production. In the early 1940s, a group of NRRL scientists, no doubt in close contact with their colleagues at the local distilleries, began a search for yeasts or molds that produced higher levels of amylases, the enzymes that break starch down into the simple sugar glucose (dextrose). The Fermentation Division and Engineering Division eventually came up with new strains of mold (*Aspergillus niger* NRRL strains 330 and 337) that produced high levels of amylases in submerged cultures, thus enabling the conversion of cornstarch to glucose much more cheaply on a large industrial scale (7). As a result, the corn processing industry could meet increased demand for corn sugar without costly expansion of facilities. For this accomplishment, the Fungal Amylase team received the USDA Superior Service Unit Award in 1956. The process is still important in the commercial production of fuel ethanol from starch. One remaining drawback



Members of the fungal amylase team at the time of their Superior Service Award in 1956.

was the presence of significant glucosyltransferase activity, resulting in unacceptable levels of unfermentable isomaltose. The problem was solved by Dr. Karl Smiley of the Fermentation Laboratory with the discovery in 1963 of a strain of *Aspergillus awamori* that produced high levels of glucoamylase with little or no transferase activity. The enzyme research also resulted in a technique eventually developed in Japan and later adopted and modified by industry for production of high-fructose corn syrups. This syrup now sweetens hundreds of products, including many fruit drinks and practically every soft drink. The fungal alpha-amylase/glucoamylase process is still important in the commercial production of fuel ethanol from starch.

An early leader of the Starch and Dextrose Division was Dr. Roy L. Whistler. Most carbohydrate scientists are familiar with the name, as Professor Whistler is famous to the point of having established the Whistler Center for Carbohydrate Research at Purdue University and the Whistler International Award for Carbohydrate Chemistry administered by the International Carbohydrate Organization, which he helped charter in 1980. The Whistler Hall of Agriculture at Purdue University is named in his honor. While Whistler is usually associated with Purdue, where he spent most of his scientific career on the faculty, it is less well known that one of his first jobs was to assemble and lead a team of carbohydrate scientists in Peoria when the NRRL first opened (8). Near the end of 1940 Whistler accepted a position there as leader of the Starch Structure Group, where he worked until 1946. It was only after his nearly six years at NRRL that he moved to West Lafayette, Indiana to take up a post at Purdue University.

The role Dr. Whistler played in establishing NRRL as a center for excellence in carbohydrate research illustrates an important point. It is impossible to separate contributions in the history of science from the individuals responsible for them. Although most of the major accomplishments at NRRL have been team efforts, those teams often were led, inspired, and sometimes driven by a strong key individual. This is particularly true in the case of Dr. Allene R. Jeanes. From her early days at NRRL

working with Whistler until long after her retirement in 1976, Jeanes played a prominent role in making NRRL a world-class center for applied carbohydrate science.

Born in 1906 in Waco, Texas, Allene Rosalind Jeanes earned an A.B. degree in chemistry from Baylor University, graduating *summa cum laude* in 1928 (9). She then went on to study organic chemistry at the Uni-



Drs. Allene Jeanes and Carl Wilham, discussing dextran research, in 1955.

versity of California at Berkeley, earning her master's degree just one year later. For the next five years she taught science at Athens College in Alabama. Traveling to the Midwest, she eventually continued her graduate work at the University of Illinois under the tutelage of the highly respected organic chemist Roger Adams. In 1938 she received her Ph.D. but subsequently encountered difficulty obtaining a suitable position with a pharmaceutical firm in her chosen field of medicinal organic chemistry. During the Depression era, employers were reluctant to hire women, especially when so many men were out of work, but she eventually found employment

in the laboratory of the famous carbohydrate chemist Claude S. Hudson. Working with Hudson at the National Institutes of Health in Washington, DC, Jeanes was funded by one of the first Corn Industries Research Foundation fellowships. She later worked with Horace S. Isbell at the National Bureau of Standards, also in Washington, further establishing her credentials as a carbohydrate chemist. It is likely that she met Whistler at that time.

When the NRRL began recruiting staff, Jeanes accepted a job back in Illinois with Dr. Whistler. It is noteworthy that in an era of open discrimination against women in the workplace, these prominent carbohydrate scientists, all in the employ of the U.S. government, saw fit to mentor a female scientist and provide her the opportunity for what would become a very productive career. (As a side note, it is also of interest to note that Hudson, Wolfrom, Isbell, and Whistler all have prestigious awards in the field of carbohydrate chemistry named after them).

While studying the acid-catalyzed hydrolysis of starch to glucose, Jeanes noted, as had many of her pre-

decessors, that a small but significant proportion of the starch was not converted to glucose, but instead gave rise to a two-glucose unit (disaccharide) “reversion” product known as isomaltose. Because isomaltose is slightly bitter, it is undesirable in corn-based sweeteners. It is also more difficult to ferment to alcohol. The problem of isomaltose formation intrigued Jeanes, but to study it, she needed a good source of isomaltose to use as a standard. It was known at that time that dextran, a bacterial slime, contained glucose chemically linked in the same manner as isomaltose (via α 1-6 linkages). To obtain large amounts of isomaltose, Jeanes began to produce dextran in her laboratory from *Leuconostoc mesenteroides* NRRL B-512, subsequently hydrolyzing it to isomaltose. This strain was originally isolated by Dr. Robert G. Benedict of the Fermentation Laboratory from a locally-produced bottle of “ropy” root beer.

Later, Jeanes and her coworkers discovered a convenient source of an enzyme to break down dextran. This came from the *Penicillium* molds whose spores were probably by then floating about the building. This process led to a convenient source of isomaltose for her group’s studies on starch hydrolysis, but more importantly, it introduced Jeanes and her co-workers to the world of dextrans and microbial polysaccharides.

In the mid to late 1940s, Swedish researchers had reported that dextran showed promise as a viscosity-enhancing agent for use in blood plasma substitutes. There were still problems to overcome, however, including the occasional anaphylactic shock reaction, inconsistencies in preparations, and difficulties in obtaining the desirable properties, to name a few. Jeanes was well aware of this work, and when the U.S. entered the Korean War in 1950, she proposed a high-priority project to develop a suitable source of dextran for use as a blood plasma extender. After an extensive survey of dextran-producing bacteria, involving the efforts of nearly 80 scientists and technicians, Jeanes and her colleagues developed the strain and techniques still used today for the commercial production of dextran (9). As it turned out, the best strain was an isolate from the NRRL B-512 culture originally found by Benedict. This work resulted in the saving of countless lives, not only on the battlefields of Korea, but to this day in emergency rooms around the world. For their accomplishments, the Dextran Team received a USDA Distinguished Service Award in 1956, and Dr. Jeanes was awarded the Francis P. Garvan-John M. Olin Medal from the American Chemical Society that same year. [Coincidentally, the Garvan Medal was established in 1936 to recognize distinguished service

to chemistry by women chemists by Francis P. Garvan, who was the chief benefactor of the NFCC, eventually leading to the formation of the USDA Regional Research Laboratories (2)].

Building on Success: The 1960s and ‘70s

Inspired by her own studies on dextran, Jeanes used what she had learned to attack another problem. One part of the NRRL mission is to develop domestically produced replacements for imported commodities. For many years, a small but valuable import from relatively unstable parts of Asia, Africa, and the Middle East had been what are known as plant gums. These complex carbohydrates are used as binders and thickeners in foods and in some industrial applications. Jeanes saw that dextrans and other microbial slimes, or gums, possessed similar properties to these imported plant gums. She reasoned that it would be possible to find a microbial gum with suitable properties that could be used in the same applications as imported plant gums. Again, after extensive surveys and extensive research in the laboratories and pilot plant, her team came up with a winner. Most of the microbiological work and fermentation studies were carried out by Dr. Martin Cadmus of the Fermentation Laboratories. The bacterium *Xanthomonas campestris* was found to generate copious amounts of a gum from glucose that was superior to such imported materials as gum tragacanth. First reported in the early 1960s, xanthan was eventually developed as a commercial product by Kelco Corporation and is now produced by numerous companies around the world. It can be found in many prepared foods as a thickener, stabilizer, and binding agent; it also finds a number of non-food industrial uses such as extending the life of oil and gas wells (10). This work was recognized by the USDA in 1968, when the Biopolymer Research



Drs. Clarence Knutson and Paul Sandford working on xanthan and other microbial polysaccharides in 1971.

Team was given a USDA Superior Service Award. In 1976 the Institute of Food Technologists presented the NRRL and Kelco Co. with the Food Technology Industrial Achievement Award for "Xanthan gum, a microbial polysaccharide with thickening, suspending, emulsifying, and stabilizing properties."

Byproducts of the work on microbial polysaccharides include the first descriptions of the unusual disaccharides leucrose (11) and isomaltulose (12), and development of a novel phosphomannan from the yeast *Hansenula holstii* (13). Isomaltulose, known commercially as palatinose, is currently being marketed as a low-glycemic sweetener (14). Phosphomannan has been used in biomedical research as an affinity ligand for mannose-6-phosphate receptors and for studying insulin-like growth factor II. The easily obtained diester cleavage product, pentamannose monophosphate, is being used as a source of the investigational anticancer drug PI-88 (15).

Jeanes retired from the USDA in 1976, but continued her work as a mentor, collaborator, and source of much knowledge for at least another decade, for despite her physical frailties in later years, her mind remained sharp. She passed away in Champaign-Urbana, Illinois in December, 1995. Jeanes was inducted into the ARS Hall of Fame in 1999.

It may be that the US government was one of the few places women and minorities could readily find gainful and productive employment as scientists at that time, because John Hodge, an African-American chemist, born in 1914 in Kansas City, Kansas, also began his career at NRRL. His father had obtained a master's degree in physics and taught at a prestigious, although segregated, high school in Kansas City. It was his father's influence as an educator with high standards that instilled the ideals of education, hard work, and excellence in young John Hodge. After graduating from the high school where his father taught, Hodge attended the University of Kansas at Lawrence, receiving a bachelor's degree in mathematics in 1936 and distinguishing himself as a Phi Beta Kappa scholar. He taught mathematics and chemistry while continuing his graduate studies and earned an M.S. in organic chemistry at Kansas in 1940. As was the case with Jeanes, he found a job at the newly opened NRRL in 1941, where he was first involved with studies on the conversion of starch to glucose. His work took a somewhat different direction, though, as he became interested in the so-called "browning reactions." When glucose comes in contact with amino compounds, including proteins, under certain conditions, the two combine

to form brown-colored products. The reactions, known collectively as the Maillard reaction(s), were poorly understood at that time. Maillard products can be desirable, as in the case of nicely browned bread or dinner rolls, or they can be undesirable, as in the case of off-color corn syrup. The products also impart distinct odor and taste to mixtures, so they are very important in the food industry. John Hodge made it his life work to study and thoroughly understand the complex browning reactions, and he made extremely important contributions to the field (16). Since this type of work did not result in a tangible invention or product, Hodge is not well-known outside his own field of expertise. However, the body of knowledge he contributed through his publications will stand for many years as the definitive word in the field. His influence also extended not only to the scientists he mentored, but to his role in encouraging and mentoring African-American students in Peoria. He was well-known and highly respected for his many community activities, even by local citizens who had no idea of his stature as an internationally known scientist. Hodge passed away in Peoria in 1996, just a month after the death of Allene Jeanes.

If the scientists in Peoria who were contemporaries of Whistler, Jeanes, and Hodge can be considered the first generation, then the second generation would include those who were attracted to NRRL because it had earned a reputation as a center of excellence in carbohydrate research. Many of these second generation scientists have recently retired or are eligible to do so, and it is from them that the authors of this article have learned not only a great deal of carbohydrate chemistry, but also some of the history of NRRL, especially with regard to personalities and reputations. This second generation includes such distinguished scientists as George Inglett, George Fanta, William Doane (a former student of Whistler), Charles Russell, Michael Gould, and Morey Slodki.

Dr. Morey E. Slodki came to NRRL just before the dextran project ended, and one of his first contributions was as part of the team that developed phosphomannans. Actually, Slodki and Jeanes first looked at yeast mannans before shifting to bacterial xanthan. However, unlike xanthan, the sensitivity of the viscosity of phosphomannan to salts precluded its use as an industrial thickener. Slodki, considered the leading figure in the development of yeast phosphomannans, is still sought out for his expertise in that field, despite having been retired since 1989. He also made substantial contributions to a better understanding of the complex structures that make up the family of dextrans and related polysaccharides. As

Jeanes' successor, he supplied samples of various dextrans and mannans to researchers in medicine, academia, and industry for many years. Some three decades after the dextran project, he used the then-new technology of capillary GC-MS, coupled with methylation analysis, to reexamine many of the dextran structures. His work, which is considered the most definitive to date, provided important data for the interpretation of immunochemical properties of dextrans. The dextran and phosphomannan collection kept at NCAUR is still an important resource for scientists around the world.

Continuing the Tradition: 1980s to the Present

"Fluffy cellulose" was developed by J. Michael Gould and co-workers in 1983. It was produced from lignocellulose from corn cobs, oat hulls, and other agricultural residue by way of a patented alkaline peroxide reaction (17, 18). Fluffy cellulose achieved important dietary objectives by providing a noncaloric, high-fiber additive for baked goods. For this work the team received the Federal Laboratory Consortium Award for Excellence in Technology Transfer as well as the R&D 100 Award.

Starch continues to be an important focus of research in Peoria, and the more recent generations of scientists continue to make major advances in its applications. In the early 1970s, Doane, Fanta, Ollidene Weaver, Ed Bagley, and their colleagues developed copolymers of starch that were capable of absorbing up to 1,000 times their weight of water (19-21). The super-absorbent copolymer, having become known as SuperSlurper, has been used in applications ranging from disposable diapers to fuel filters. SuperSlurper was based on the starch grafting technology pioneered by Charles Russell (22). ARS



SuperSlurper inventors William Doane, George Fanta, and Mary O. Weaver, early 1970s.

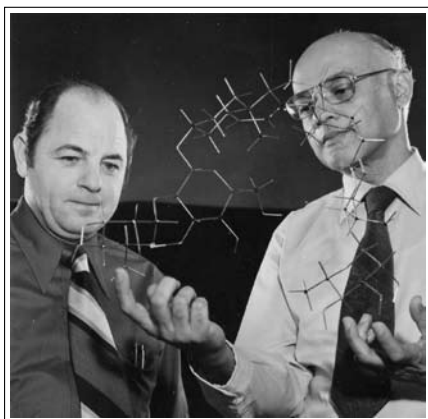
has granted over 40 nonexclusive licenses to make, use, or sell SuperSlurper (23). The team continued to work with industry to transfer the technology and earned the Inventor of the Year Award from the Association for the Advancement of Invention and Innovation and the USDA Distinguished Service Award in 1976. Doane and Bagley were inducted into the ARS Hall of Fame in 1995 and 2003, respectively. These same scientists have contributed many other developments besides SuperSlurper, including starch derivatives that have been used in the paper industry and waste water treatment, as well as a patent filed by Weaver and Russell for novel carbohydrate aliphatic and cyclic acetals in 1966 (24).

More recently, George Fanta and the late oil chemist Ken Eskins were responsible for the invention of a stable oil-water-starch emulsion that is being developed for a myriad of uses in food, medicine, and industry under the name Fantesk (25). Fanta and Doane have also received numerous awards from outside organizations, including the ACS, for their contributions to carbohydrate chemistry.

Another major contributor to the reputation of the Peoria USDA laboratory as a center of excellence has been Dr. George E. Inglett, who had already established himself as a successful scientist before coming to Peoria. When Inglett was honored as Chemist of the Year by the Illinois Heartland local section of the ACS in 2005, he stated that one of the influential factors in his life was the death of his best childhood friend from food poisoning during the Great Depression. During his scientific career Inglett has dedicated himself to the development of a safer and more healthful food supply. He received his B.S. in Chemistry from the University of Illinois in 1949 and his Ph.D. in biochemistry from the University of Iowa just three years later. He worked for many years in the agro-food industry, researching natural sweeteners, among other things. In 1967, when the size of the NRRL was increased 50% by addition of a new wing, he accepted a position as Chief of the Cereal Properties Laboratory. Inglett has continued his career as a food chemist since then and is best known for the development of a family of food ingredients based on cereal glucans, known collectively as the Trim Technologies (26-28). These ingredients are used as fat substitutes, fiber additives, texturizers, and emulsion stabilizers in many foods. OatTrim entered the market a record two years after its discovery and has been licensed by Quaker Oats and Rhodia. These developments have allowed Inglett to realize his lifelong goal of a more healthful food supply by providing consumers with high fiber, low fat, and

low glycemic processed foods. For his contributions as a USDA scientist, Inglett was inducted into the ARS Hall of Fame in 2002. The Institute of Food Technologists has honored Inglett with the Industrial Scientist Award and Babcock-Hart Award for contributions to food technology, which have resulted in improved public health through nutrition or more nutritious food in 2000 and the Nicholas Appert Award for preeminence in and contributions to the field of food technology in 2006. In 2005 Inglett was chosen as one of the Laureates of The Lincoln Academy of Illinois, the highest honor the State of Illinois can bestow on persons who were born or have resided in Illinois for outstanding achievement. Inglett has been presented with many awards and honors from several other organizations, far too numerous to list here.

The current generation of carbohydrate scientists in Peoria has inherited a great deal of inspiration from those who have gone before them, building on their successes in the conversion of crop-based carbohydrates to value-added products. A large number of the hundred or so scientists at NCAUR are investigating ways to convert crop-derived carbohydrates such as cellulose and hemicelluloses to fuel ethanol. A somewhat smaller group has been dedicated to preserving the functionalities of the carbohydrate molecules while converting them to new materials. The chemists in the Plant Polymer Research Unit (PPL), for example, focus on derivatizing starch and protein through chemical and physical processes to make new polymers for use in the plastic industry. Chemists and biochemists in the Bioproducts and Biocatalysis Research Unit (BBC) take a somewhat different approach, using enzymes to produce novel compounds from starch, sugar, hemicelluloses, and other starting materials. One recent product arising from BBC research, sucromalt, is currently marketed as a low-glycemic sweetener for diabetics and in sustained-release energy bars and drinks.



Drs. George Inglett and John Hodge in 1973.

Where NCAUR Fits into our Nation's Future

In 1990 the ACS recognized the contributions of all four of the original Regional Research Laboratories and presented them with plaques that read, in part, "In Appreciation of 50 Years of Contributions to Carbohydrate Chemistry and to the Division." The current generation respects the contributions of those who established the reputations of our laboratories and hopes to make the next 50 years equally successful.

To put the contributions of the USDA as a whole and NCAUR in particular in perspective, it is helpful to understand how the Department and Center fit into the national research picture. Since 1953 NCAUR has been administered by the Agricultural Research Service (ARS), the USDA's in-house research agency. ARS research is funded at approximately \$1.1 billion for fiscal year 2008, and the money is allocated to research programs according to program areas. The bulk of NCAUR funding, totaling approximately \$30 million for FY2008, falls under the two program areas of Bioenergy Research and Agricultural Product Utilization and Quality Research. In the most recent fiscal year, The National Science Foundation (NSF) had a budget of about \$6 billion, which was allocated entirely through grants. The National Institutes of Health, which has a history as long and interesting as USDA, funds research both in-house and through extramural grants, with a FY2008 budget of approximately \$28 billion. The Department of Energy (DOE), which runs in-house laboratories through contracts, as well as funding extramural grants, has a total annual budget for its Office of Science of approximately \$4 billion, with about \$200 million of that going to biomass and biorefinery research. As one can see from these figures, in the grand scheme of things, the ARS budget, including NCAUR, is a relatively small slice of federal R&D funding. Despite this fact, the contributions of ARS and NCAUR to the national economy have been significant. Part of the reason for such a highly successful history is due to the fact that NCAUR scientists have recognized the value of collaborations to succeed in their work. In the past, this was exemplified by cooperation between the War Department and USDA during the penicillin and dextran projects and between NIH and NCAUR in subsequent years, as NIH continued to study dextran-specific antigens. The USDA and DOE currently coordinate many of their efforts in the areas of biofuels research and biomass conversion. NCAUR scientists also have good working relationships with fellow scientists in most of the other 100 or so ARS facilities. However,

by far the most significant of NCAUR's collaborations have always been with the private sector. The goal of utilization research is to create new markets, and so the entire process from conceptualization to product development depends strongly on such interactions. NCAUR has established itself as a leader in public-to-private technology transfer, as demonstrated by its long list of awards for these accomplishments. USDA agricultural research, as exemplified by the Regional Research Centers, including the Peoria laboratory, has a long established history of contributing to our nation by developing new technologies which have strengthened our farm economy. In addition, it has provided the world a more healthful food supply, new medicines, new plastics, and a more productive industrial base.

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REFERENCES AND NOTES

*The use of brand or trade names may be necessary to report factually on available data. The USDA neither guarantees nor warrants the standard of the product, and the use of the name by USDA implies no approval of the product to the exclusion of others that may also be suitable. All programs and services of the USDA are offered on a nondiscriminatory basis without regard to race, color, national origin, religion, sex, age, marital status, or handicap.

1. Anonymous, *USDA Employee News Bulletin, Centennial Edition*, May 9, 1962.
2. M. R. Finlay, "Old Efforts at New Uses: A Brief History of Chemurgy and the American Search for Biobased Materials," *J. Ind. Ecol.*, **2004**, *7*, 33-46.
3. H. W. Kelley, *Always Something New. A Cavalcade of Scientific Discovery*, USDA-ARS Misc. Pub. 1507, Washington, DC, 1973.
4. ACS National Historic Chemical Landmarks Program <http://acswebcontent.acs.org/landmarks/>
5. S. Aldridge and J. L. Sturchio, *The Discovery and Development of Penicillin 1928-1945. An International Historic Chemical Landmark*, Am. Chem. Soc. and Roy. Soc. Chem., 1999.
6. A. J. Moyer, "Method for Production of Penicillin," *U. S. Patent 2,476,107*, 1949.
7. E. H. LeMense, J. Corman, J. M. VanLanen, and A. F. Langlykke, "Production of Mold Amylases in Submerged Culture," *J. Bacteriol.*, **1947**, *54*, 149-159.
8. J. N. BeMiller, "Professor Roy L. Whistler," *Carbohydr. Res.*, **1979**, *70*, 179-184.
9. P. A. Sandford, "Allene R. Jeanes," *Carbohydr. Res.*, **1978**, *66*, 3-5.
10. Anonymous, "Xanthan Gum Offers Versatility, Safety," *Food Technol.*, **1974**, *28*, 18-21.
11. F. H. Stodola, H. J. Koepsell, and E. S. Sharpe, "A New Disaccharide Produced by *Leuconostoc mesenteroides*," *J. Am. Chem. Soc.*, **1952**, *74*, 3202-3203.
12. F. H. Stodola, E. S. Sharpe, and H. J. Koepsell "Leucrose and isomaltulose in the dextran synthesis," *Abstr. Nat. Meeting, Am. Chem. Soc., Carbohydr. Div.* 5D, 1954.
13. R. A. Anderson, M. C. Cadmus, R. G. Benedict, and M. E. Slodki, "Laboratory Production of a Phosphorylated Mannan by *Hansenula holstii*," *Arch. Biochem. Biophys.*, **1960**, *89*, 289-292.
14. B. A. R. Lina, D. Jonker, and G. Kozianowski, "Isomaltulose: A Review of Biological and Toxicological Studies," *Food Chem. Toxicol.*, **2002**, *40*, 1375-1381.
15. V. Ferro, K. Fewings, M. C. Palermo, and C. Li, "Large-scale Preparation of the Oligosaccharide Fraction of *Pichia holstii* NRRL Y-2448 Phosphomannan for Use in the Manufacture of PI-88," *Carbohydr. Res.*, **2001**, *332*, 183-189.
16. J. E. Hodge, "Chemistry of Browning Reactions in Model Systems," *J. Agric. Food Chem.*, **1953**, *1*, 928-943.
17. J. M. Gould, "Alkaline Peroxide Treatment of Nonwoody Lignocellulosics," *U. S. Patent 4,649,113*, 1987.
18. M. S. Kerley, G. C. Fahey, Jr., L. L. Berger, N. R. Merchen, and J. M. Gould, "Effects of Alkaline Hydrogen Peroxide Treatment of Wheat Straw on Site and Extent of Digestion in Sheep," *J. Anim. Sci.* **1986**, *63*(3), 868-878.
19. M. O. Weaver, E. B. Bagley, G. F. Fanta, and W. M. Doane, "Highly Absorbent Starch-Containing Polymeric Compositions," *U. S. Patent 3,981,100*, 1976.
20. M. O. Weaver, E. B. Bagley, G. F. Fanta, and W. M. Doane, "Highly Absorbent Starch-Containing Polymeric Compositions," *U. S. Patent 3,997,484*, 1976.
21. G. F. Fanta, E. I. Stout, and W. M. Doane, "Highly Absorbent Graft Copolymers of Polyhydroxy Polymers, Acrylonitrile, and Acrylic Comonomers," *U. S. Patent 4,124,863*, 1979.
22. Z. Reyes and C. R. Russell, "Graft Polymerization of Starch Ion Novel Alcohol Reaction Medium," *U. S. Patent 3,518,176*, 1970.
23. L. Cook, "One Team, One Product - Many Uses," *Ag Research Magazine*, May, 1996, 10-13.
24. M. O. Weaver and C. Russell, "Carbohydrate Aliphatic and Cyclic Acetals," *U. S. Patent 3,294,781*, 1966.
25. K. Eskins and G. F. Fanta, "Non-separable Starch-oil Compositions," *U. S. Patent 5,676,994*, 1997.

26. G. E. Inglett, "Method for Making a Soluble Dietary Fiber Composition from Oats," *U. S. Patent 4,996,063*, 1991.
27. G. E. Inglett, "Method of Making Soluble Dietary Fiber Compositions from Cereals," *U. S. Patent 5,082,673*, 1992.
28. G. E. Inglett, "Dietary Fiber Gels for Calorie Reduced Foods and Method for Peparing the Same," *U. S. Patent 5,766,662*, 1998.

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Editor's Note: This feature is being introduced for the first time in this issue. It was suggested by founding editor of the BULLETIN, William B. Jensen, Curator of the Oesper Collections at the University of Cincinnati. We hope this will become a continuing item in future issues of the journal.

LOST ARTIFACTS? The Squibb Museum

Among the books in the Oesper Collections is a small 4.5" x 7" volume of 190 pages by George Urdang and F. W. Nitardy bound in brown leatherette and titled *The Squibb Ancient Pharmacy: A Catalogue of the Collection*. Published in 1940 by E. R. Squibb and Sons of New York, it describes in some detail the artifacts in a two-room museum of pharmacy located on the 28th floor of Squibb Building at the corner of 58th Street and 5th Avenue. Purchased from a private collector in Europe by Squibb and brought to the United States in 1932, one room of the museum was arranged like a Baroque pharmacy and the second as a laboratory or "Faust study" containing a reproduction of a period furnace and hood. Most of the collection appears to have consisted of highly decorated period pharmacy containers, spanning the 15th through the early 19th centuries, and a large collection of mortars and pestles, some dating back to the 7th century. In addition, there were rare books, framed prints (many of which I have never seen elsewhere), paintings, sculpture, and some apparatus common to both pharmacy and chemistry, including 18th-century balances, a microscope, glass alembic heads, and several Florentine distillation receivers. I can find nothing about this museum on the internet, and presumably the Squibb Company has long since been absorbed by some larger pharmaceutical conglomerate. My question is whether any of the readers of the *Bulletin* have any idea what happened to this museum and to its valuable contents.

Readers having information relating to the above artifacts or questions of their own which they would like to see addressed in future columns should send their comments and questions to Dr. William B. Jensen, Department of Chemistry, University of Cincinnati, Cincinnati, OH 45221-0172 or email them to Jensenwb@email.uc.edu.

BOOK REVIEWS

Chymists and Chymistry. Studies in the History of Alchemy and Early Chemistry. Lawrence M. Principe, Ed., Science History Publications, Sagamore Beach, MA, 2007, xiii + 274 pp, ISBN 0-88135-396-5, \$45.

George Sarton was largely responsible for the establishment of the history of science as an academic discipline. He founded the journal *Isis* in 1912 and continued crusading for the subject until his death in 1956, the year I entered the graduate program at Harvard University. For the handful of graduate students at that time the history of science seemed to be dominated by the astronomy and physics of motion of the sixteenth and seventeenth centuries. This was an approach in tune with Sarton, who believed that the maturity of a science was dependent on the extent to which it had been mathematicized. Accordingly, little time was spent in our courses and seminars on chemistry or the biological sciences while medicine was completely ignored. As a chemist myself, I was disappointed with this approach; and I soon found that chemical and iatrochemical texts formed a very large part of the literature of the Scientific Revolution. Although important research had been carried out in the study of alchemy and early chemistry, relatively little of this had affected the history of science as a whole.

Over the past half century there has been an ever increasing number of scholars investigating the development of chemistry. An international conference on alchemy and early chemistry was held at Groningen in 1989 and a second one in Philadelphia at the Chemical Heritage Foundation in 2006. The present volume

includes many of the papers from the latter meeting and presents the reader with a much needed overview of the present state of this field of research. One name that appears frequently throughout the volume is Paracelsus, the firebrand sixteenth-century Swiss-German reformer who sought to make chemistry a part of medicine. Much current Paracelsian research is centered on his followers and their debates. Here Didier Kahn discusses the French Paracelsians at the Court of Henry IV, while Bruce T. Moran presents a paper on the German enemy of mysticism, Andreas Libavius. A proponent of Aristotelian logic and philosophy, Libavius accepted traditional alchemical texts while rejecting Paracelsian mysticism. Stephen Clucas touches on some of the same points in his paper. Referring again to Libavius, Clucas points to his attack on the obscurity of language in alchemical texts as well as their confusion of chemistry and religion. Peter Forshaw turns to Heinrich Khunrath in his paper, whom he shows to have been concerned with laboratory practices even though he has frequently been dismissed as a mystic.

Dane T. Daniel is concerned with the reception of Paracelsian theology among his early followers. A related paper is that of Margaret D. Garber, who contrasts the differing views of matter theory upheld at the University of Prague by J. Marcus Marci and the Jesuit, Roderigo Arriaga. In this case the concept of *semina* presented a problem for the understanding of the Eucharist.

Hiro Hirai presents a paper on Athanasius Kircher's views on the Creation and spontaneous generation, which he shows to have been derived from Paracelsian chemical concepts, Marcus Marci's optical theory of plastic power,

and the corpuscular views of a largely neglected Padual physician, Fortunio Liceti. William Newman shows the influence of another seldom mentioned author, in this case Johann Grasseus, whose views on the generation of metals influenced Isaac Newton.

Other papers reflect more traditional research in alchemical subjects. Wouter J. Hanegraaf follows his own and Ruud M. Bouthoon's earlier work on Ludovico Lazzareli in the examination of the mercurial phoenix and its miraculous powers as the philosophers' stone. Barbara Obrist describes the alchemical significance of an early sixteenth-century miniature painting by Jean Perréal. The sexual metaphors found in alchemical texts are the subject of Allison B. Kavey's offering, while Gabriele Ferrario compares the Arabic and Hebrew versions of the *Liber de aluminibus et salibus*, which was translated into Latin by Gerard of Cremona in the twelfth century. An interesting paper by Tara Nummedal discusses alchemical fraud and in particular, the case of Heinrich Nüschler, who was eventually hanged (1601) because of his failure to carry out a successful transmutation. Nummedal emphasizes the importance of contracts made between alchemists and their patrons.

The laboratory practice of early modern chemistry is discussed in two papers. In the first, Marcos Martín-Torres shows that the finest crucibles in the sixteenth and seventeenth centuries came from two areas, Hesse and Bavaria. The equipment of a Paracelsian laboratory is described by R. Werner Soukup from discoveries made during the excavations at Castle Oberstockstall in Austria.

The book ends with seven papers related to late seventeenth- and eighteenth-century chemistry. The first three deal with chemistry in the French Academy of Sciences. Victor D. Bonantza discusses the reaction of Samuel Cottureau Duclos to the work of Robert Boyle. His work shows the influence of corpuscular and mechanical thought as well as a continuing interest in traditional vitalism. Luc Peterschmitt presents a paper on the Cartesian impact on chemistry through the texts of Gérard de Cordemoy, Jacques Rohault, and Pierre-Sylvain Régis. In the end he concludes that "Chemistry turned mechanism into a problem, because chemistry is a limit for mechanism" (p 201). In his paper Bernard Joly turns to a long-running debate in the Academy between

Etienne François Geoffroy and Louis Lemery regarding the possibility of preparing an artificial iron.

John C. Powers offers a paper on the alchemical interests of Hermann Boerhaave, while Kevin Chang turns to Georg Ernst Stahl. Historians of chemistry have presented Stahl primarily as the originator of the phlogiston theory and have paid little attention to his voluminous other work. Here Chang writes of Stahl's change from a belief in transmutation to disbelief. Other works by him show that he rejected the vital influence of the celestial to the terrestrial worlds indicating a major shift away from the vitalistic cosmology. Another shift in thought is to be found in Hjalmar Fors' contribution on the Swedish Board of Mines. In his discussion of the work of Georg Brandt and Fredrik Cronstadt he illustrates the gradual move from a Paracelsian emphasis to a reliance on Boerhaave, Descartes, and Newton.

Anyone who has spent time with the alchemical bibliographies of Ferguson or Duveen is well aware that the eighteenth century was a time of continued strong interest in alchemical and Paracelsian texts. Claus Priesner touches on some of this material in his paper on two eighteenth-century German secret societies: the Gold- and Rose-Cross and the Illuminati. There is little doubt that there is still much to be done in this area—not only to understand its continued appeal in the period of the Enlightenment, but also to indicate its connection with the Romantic movement, a subject in which David Knight has contributed so much for the English scene over the past half century.

The present volume reflects the breadth of current interest in pre-Lavoisier chemistry and alchemy. Because of this I have already recommended it to several prospective graduate students in the field. If there is any weakness in the collection, it may be to give adequate recognition to the work and influence of J. B. van Helmont or to reflect the intricate connection between chemistry, pharmacy, and medicine in this period. The latter was a legacy of the late medieval distillation books and the vast Paracelsian and iatrochemical literature. Regardless, this is a very important book; and we may congratulate the editorial work of Professor Principe, the production skills of Science History Publications, and the support of the Chemical History Foundation. *Allen G. Debus, The University of Chicago.*

Robert Wilhelm Bunsens Korrespondenz vor dem Antritt der Heidelberger Professur (1852): Kritische Edition. Christine Stock, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 2007. (Quellen und Studien zur Geschichte der Pharmazie, F. Krafft and C. Friedrich, Ed., Vol. 83). cxlviii + 610 pp., ISBN 978-3-8047-2320-7, € 49.

Christine Stock rightly notes in her introduction that Robert Bunsen (1811-1899) “was one of the most significant scientists of the nineteenth century” (p xxiii). Of the great figures of that century, he was also one of the most prolific, influential ... and, until now, least studied by historians. The invaluable critical correspondence edition under review here reproduces all known letters or documents to or from Bunsen bearing dates from September 27, 1830 (the earliest such document known) until August 15, 1852, his last surviving letter before he moved to Heidelberg to take up his new professorship there. The letters thus span the periods he spent in Göttingen (as student and then Privatdozent, 1830-36), in Kassel (as Friedrich Wöhler’s successor at the School of Trades, 1836-39), in Marburg (as *ausserordentlicher*, then *ordentlicher* Professor, 1839-51), and finally in Breslau for three semesters as professor at the Prussian University (1851-52). These letters are currently held in thirty-three different archives in Germany, England, France, Sweden, Italy, and Poland.

Some years before his death in 1899 Bunsen consigned his entire correspondence files to the flames, and in his will he directed his executor to destroy all letters and other papers that had inadvertently escaped this fate. Fortunately, that executor—Philipp Bunsen—could not bring himself to follow these instructions for the few letters he found in his uncle’s effects. Moreover, although he felt bound by the will not to take any steps to publish these remaining letters himself, Philipp raised no legal barriers to others’ taking such actions. In this way, 56 letters to Bunsen from the stated period survived to be included in this edition, along with 246 letters from Bunsen to various correspondents—for, of course, Bunsen had no power to destroy letters that were in the possession of his friends and colleagues. These 302 transcribed letters are supplemented by 164 interpolated headings for additional specific Bunsen letters known to have once existed (e.g., because they were mentioned in surviving letters as having been received). Stock’s final entry, a letter from Bunsen to Eilhard Mitscherlich in August 1852, is therefore numbered the 466th of this edition. The edition includes many important letters, the majority hitherto unpublished, to or from Jacob Berzelius, Hein-

rich Debus, Edward Frankland, Hermann Kolbe, Justus von Liebig, Mitscherlich, Jules Pelouze, Lyon Playfair, Victor Regnault, John Tyndall, Friedrich Wöhler, and many others.

If only all correspondence editions were conducted with such scrupulous care and editorial professionalism as is found here! The letters appear *verbatim et literatim*, and readers can rely on the accuracy of the transcriptions, down to the minutest detail. For each letter the editor provides a complete physical description, current location, citations to any previous publication of (or even published reference to) the item, commentary or necessary identifications in footnotes, and a list of changes in draft by the original author or emendations by the editor. Stock was indefatigable in tracking down even the most minor references. Her energy and accuracy can be exemplified by the 37 (!) different personal names with the patronymic “Bunsen” that are fully referenced in her name index; or (for instance) Bunsen’s casual allusion to the “Römischer Kaiser” in one letter (p 306), which Stock succeeds in identifying as the name of a former inn on the Gouvernementplatz in Kassel. Consequently, if one reads the annotation “bislang nicht identifiziert” in a footnote, one may assume that much expert effort has been frustrated there!

Despite the editor’s admirable diligence, we can infer that what we have here is only a small fraction of what once existed. For example, in one missive (p 441) Bunsen apologized for his poor handwriting, for, he said, this was the tenth of twelve letters that he needed to write that day; however, of the twelve, only the letter that contains this reference has survived—and these were outgoing letters, immune from his epistolary pyromania. Nonetheless, the present volume still provides us an extraordinarily clear picture—and the best we are likely to get—of Bunsen’s doings, especially regarding his research and his dealings with university administrations. Moreover, Stock obviously mastered Bunsen’s entire unpublished correspondence, including the ca. 500 surviving letters to or from our hero with dates later than August 1852, for she often interpolates material or direct quotations from these later letters, wherever appropriate. Consequently, from a close reading of this volume we gain much historical benefit from not just ca. 300, but from all ca. 800 surviving letters from Bunsen’s correspondence. (Bunsen’s post-1852 correspondence was the subject of Stephanie Hoss-Hitzel’s 2003 Heidelberg Ph.D. dissertation, but that work is disappointing and cannot compare to this one; for one thing, Hoss-Hitzel included only brief summaries, not transcriptions of the letters.)

We learn plenty from perusal of this volume. The descriptions of Bunsen's several travels, described in long letters to family members, are priceless. We avidly follow as the peripatetic 21-year-old newly-minted D. phil. tells his parents all about his Wanderjahr (actually 16 months) in Berlin, Paris, and Vienna, as well as an interesting three days spent with Liebig in Giessen at the very time of his collaboration with Wöhler on the benzoyl radical found in the oil of bitter almonds. Over 100 pages of this edition are devoted to this trip alone. Not less interesting are ground-level insights into Bunsen's work on the cacodyl radical, on physical-chemical investigations of gases, and on the geology of Iceland. Those interested in learning how German academic politics actually operated in the nineteenth century will gain new appreciation of the different ways that German governments decided upon candidates for academic posts, and how candidates conducted themselves in these searches. Until one has read these letters it has not been understood just how influential Bunsen obviously became, not only in international science but in local academic politics in his later Marburg years and in Breslau.

Finally, we can now write a much fuller account of how it was that he was lured—with great difficulty!—from Marburg to Breslau, and with what trepidation he finally went; only the repressive post-1848 political environment in Kurhessen provided the necessary push. The pull, of course, was the promise by the Prussian authorities to build him a new laboratory institute in Breslau. However, we learn here that Bunsen made this request only after officially accepting the call. His reduced bargaining leverage meant that the lab almost did not get built. The existing facilities, Bunsen wrote his friends, were worthless; his predecessor, N.W. Fischer, whom Bunsen referred to in one letter (p 522) as an “alter Esel,” had run Breslauer chemistry into the ground. This, combined with the poverty of the student body—a majority of whom were granted remission of fees, dramatically lowering Bunsen's income—was a depressing combination of circumstances.

On the eve of his departure for Breslau, the arrival of a letter from authorities in Baden offering him a professorship in Heidelberg saved Bunsen. Although he was not in a position to accept the offer—he felt morally bound to keep his promise to the Prussians—he now had the leverage he needed to get that new laboratory building. In fact, we learn that it required three separate “calls” by the state of Baden over fourteen months, before Bunsen finally overcame his scruples to accept the Heidelberg post. By the time of his departure in 1852, the new lab in

Breslau was nearly finished. But Heidelberg, having lost out to Munich in the competition to entice Liebig away from Giessen, had promised Bunsen an even bigger and better laboratory. In fact, these various calls formed the beginning point of the gradual rise of German academic chemistry to its leading European rank towards the end of the century.

Bunsen was a man of remarkable probity, modesty, and kindness, probably the most uniformly and justly admired scholar of his generation. He scrupulously avoided conflict, in both conversation and in correspondence; he used to say that one would be able to read his letters aloud in the marketplace without embarrassment. But this, we now know, was at least a slight exaggeration. In fact, he absorbed, or at least shared, many of the same aversions of the chemist whom he most revered, Berzelius. Both men thought that J. B. Dumas was foolish, insincere, and vain (pp 202, 293), and when Liebig broke with Berzelius and began to bandy insults, Bunsen offered the Swede his fullest sympathy, with private vitriol directed against the sage of Giessen (pp 271, 293, 379). In 1832 Bunsen compared many lectures in Parisian institutions to the performances of conjurers (p 67), and in 1840 expressed his low regard for academic chemistry in England, where the resplendence of the laboratories bordered on charlatantry (p 195—a complaint borne of envy, which two decades later would be echoed by the French against German laboratories!). It is however noteworthy that Bunsen's rare unbuttoned derogations are found almost exclusively in letters to Berzelius—a man whom he knew to be sympathetic, whom he venerated, and who resided in a foreign country.

The volume is fully equipped with indexes, an admirably complete bibliography, and a foreword by Fritz Krafft (who directed Stock's 2005 Marburg dissertation, which formed the basis for the present work). Most important, though, is a superb 148-page introduction that summarizes the new historical knowledge provided by this correspondence, and also (though to a lesser extent) the current state of Bunsen scholarship *tout court*, over the course of the protagonist's entire life. Extensive footnotes provide both specific detail and broader context, ranging widely across the history of science as well as the general history of the period as it pertains to the action on stage. In short, this volume provides a major new contribution to the understanding of one of the most important scientists of the nineteenth century, as well as of his partners in correspondence. *Alan J. Roche, Case Western Reserve University, Cleveland, OH 44106/USA.*

Scientific Institutions and Practice in France and Britain, c. 1700-c.1870. Maurice Crosland, Ashgate, Aldershot, Hampshire, 2007. Cloth, xvi + 270 pp, \$109.95.

The name of Maurice Crosland is well known to the history of chemistry community. Winner of the 1984 Dexter Award in the History Chemistry and the author of such classics as *Historical Studies in the Language of Chemistry* (1962), *The Society of Arcueil* (1967), and *Gay-Lussac: Scientist and Bourgeois* (1974), he is widely regarded as the world expert on 18th- and early 19th-century French chemistry. The volume under review is part of Ashgate's Valorium Collected Studies Series and consists of reprints of 12 of Crosland's most recent publications, all of which originally appeared either as papers in various journals or as book chapters in various edited volumes. As such, it is a successor to an earlier collection (*Studies in the Culture of Science in France and Britain Since the Enlightenment*) of Crosland's papers published as part of the same series in 1995. The first seven selections in the current collection deal with various institutional aspects of chemistry and science in both France and Great Britain, and the remaining five selections with various aspects of laboratory practice. Also included is a brief introduction by Crosland, a complete bibliography of his publications since the appearance of the first collection in 1995, a general index, and an attractive portrait of the author, which appears opposite the title page.

The various papers and book chapters have been reproduced as photofacsimiles of the originals rather than being reset in a uniform manner. Though the reproduction of the original printing is of high quality, the same cannot be said of many of the original illustrations, several of which resemble low grade photocopies. In addition, the publisher has retained the original pagination of each paper and, rather than adding a secondary pagination for the collection as a whole, has instead assigned each paper a Roman numeral, which is then combined with the original page numbers to create the various index entries.

So much excellent work on the history of chemistry gradually becomes lost in the back volumes of various journals, that it is a pleasure to see some of it given a fresh lease on life. Reprint volumes of this sort not only give an author's work a more permanent and focused format; they also aid its dissemination, as many smaller libraries, which are unable to afford or maintain complete runs of the journals in question, are able to afford individual volumes of this sort. In this regard, it should also be noted that Ashgate's Valorium reprint series contains several other volumes of specific interest to historians of chemistry, including collections of papers by William Brock, Trevor Levere, and the late Wilfred Farrar. Ashgate is to be congratulated in making this opportunity available to British historians of science, though it is a great pity that no similar opportunity appears to be available to American historians. *William B. Jensen, University of Cincinnati.*

New Dictionary of Scientific Biography. Noretta Koertge, Editor-in-Chief. Charles Scribner's Sons, an Imprint of Thomson Gale (now a part of Cengage Learning), Farmington Hills, MI 48331-3535, 2008; <http://www.gale.com>; hardbound, 8 vol., cxvi + 3,271 pp, ISBN 978-0-684-31320-7, \$995.

In 1965 Charles Scribner's Sons, supported by the American Council of Learned Societies, began the immense task of publishing authoritative biographies of the most important natural scientists and mathematicians who had lived up to that time. The project resulted in the

publication (1970-1980) of the 16-volume *Dictionary of Scientific Biography*, with Charles Coulston Gillispie as Editor-in-Chief. In 1990 two supplementary volumes (Volumes 17 and 18), under the editorship of Frederic L. ("Larry") Holmes, were added to include recently deceased scientists such as Rachel Carson, Kurt Gödel, Werner Heisenberg, Carl Shipp Marvel, Jacques Monod, and Gerold Schwarzenbach. The 18-volume set, hailed by Choice as "monumental" and by Booklist as "the definitive biographical source for scientists," became an indispensable educational and research tool for historians of science as well as a popular reference for high school, college, and university students and the general public.

An abridged one-volume version, *Concise Dictionary of Scientific Biography*, appeared in 1981, while a second edition (2000) included material from the 1990 supplementary volumes.

In late 2004 Noretta Koertge approached scholars for proposals of biographies to appear in a forthcoming *New Dictionary of Scientific Biography* (NDSB), again with the support of the American Council of Learned Societies. Koertge received her B.S. (1955) and M.S. (1956) degrees in chemistry from the University of Illinois, where she completed all the work for her Ph.D. in 1959. After a decade as a lecturer and professor in the United States, Turkey, England, and Canada, she received her doctorate in the philosophy of science under Heinz R. Post at Chelsea College, University of London in 1969. In 1970 she joined the Department of the History and Philosophy of Science at Indiana University and retired in 2000, as Professor Emerita. Her research interests include the history of methodology and of chemistry and the philosophy of science. She was also Editor-in-Chief of the journal *Philosophy of Science* (1999-2004).

The NDSB, with Koertge as Editor-in-Chief, aided by a nine-member advisory committee, 23 subject editors, and nine consulting editors, appeared in eight volumes. The 629 authors hail from 37 countries. In contrast to the DSB, all volumes appeared simultaneously, and they contain numerous portraits, photographs of scientists at work, and images from their publications to increase its accessibility to a general readership. The coverage now includes anthropology and psychology and, to a limited extent, some areas of economics and sociology. As was the case with the original DSB, the goal has been "to identify the most noteworthy scientists and present the story of their accomplishments within the broader context of their lives in essays that reflect the best available historiographic research," an objective that, in my opinion, has been eminently attained.

The NDSB extends, complements, and comments on the original set with 775 completely new entries. About 500 articles are devoted to scientists who died since 1950 and were not included in the DSB such as Hans Bethe, Francis H. C. Crick, Richard Feynman, Stephen Jay Gould, Fred Hoyle, Christian Klixbüll Jørgensen, Mary Leakey, Willard Frank Libby, Konrad Lorenz, Barbara McClintock, Linus Pauling, Andrei Sakharov, Burrhus Frederic (B. F.) Skinner, and Edward Teller. Seventy-five "gap" entries on scientists previously overlooked in the DSB, such as Chrysippus, Ernest Everett Just, and Alfred Kinsey, as well as 225 "postscript" commentar-

ies on important figures who have inspired new research or interpretation, such as Archimedes, Aristotle, Robert Boyle, Charles Darwin, Albert Einstein, Sigmund Freud, Hypatia, August Kekulé, Antoine-Laurent Lavoisier, and J. Robert Oppenheimer, are intended to supplement, but not to replace, the original articles in the DSB. For example, the entry on Isaac Newton's alchemy (Volume 5, pp 273-277) adds a new dimension to our understanding of his theory of matter, while the entry on (Johann) Gregor Mendel (Volume 5, pp 97-101) elucidates the surprising link between his famed pea experiments and earlier discussions of heredity that occurred at meetings of the Moravian Sheep Breeders Society.

While key figures in biology, chemistry, mathematics, and physics have not been neglected, scientists who have pioneered new disciplines that play pivotal roles in today's society are also included. To achieve this purpose special editors for cognition, computer science, decision theory, ecology, ethology, neuroscience, and space science were appointed. Traditional fields that have matured and increased in importance like climatology, physical anthropology, and psychology have been emphasized.

The increase in historical research on women in science since the publication of the DSB and the changes in the social structure of the scientific community are reflected in the greater number of entries devoted to women, e.g., Maria Gaetana Agnesi (Volume 1, pp 19-21), who wrote a famous book on calculus; Caroline Lucretia Herschel, sister of astronomer William Herschel (Volume 3, pp 286-287), who discovered several comets; Ada Augusta King, Countess of Lovelace (Volume 4, pp 118-120), who wrote the first computer program; and Maria Sibylla Merian, who contributed to botany, entomology, ethnography, and natural history (Volume 5, pp 118-120).

The DSB was criticized for its neglect of non-Western scientists; the NDSB has filled this gap by a greater emphasis on Arabic, medieval, African-American, and Asian researchers. Because our understanding of past and current science is influenced by philosophical and sociological theories about its structure and development, the NDSB contains entries on Thomas Samuel Kuhn and his notion of the paradigm (Volume 4, pp 170-177), Robert King Merton and his theory of scientific norms (Volume 4, pp 121-126), and Karl Raimund Popper and his falsifiability criterion (Volume 6, pp 133-137). Many of the new essays reflect the growing interest of historians in the social conditions and disciplinary organizations in which scientists work.

The NDSB retains the superior print, alkaline paper, design, and binding of the DSB. Although the separate volumes do not appear to be available individually, they bear different ISBNs. Biographies take up Volumes 1-7. Volume 8 contains lists of contributors, their affiliations, and article titles (25 triple-column pages); scientists by field (14 triple-column pages); Nobel Prize winners (1 triple-column page); and articles (5 triple-column pages) as well as a note on the index (2 double-column pages). The index itself comprises 208 double-column pages.

Simultaneously with the publication of the print version of the NDSB, an electronic version of the 8 volumes of the NDSB, along with the 18 volumes of the original DSB titled the *Complete Dictionary of Scientific Biography*, was published. (ISBN 978-0-684-31559-1) Since the online “e-book” version is fully searchable, users can pose questions that would elude even the best

print index. Not only will this facilitate research but can lead to new avenues of inquiry about how science works. Also, the Complete DSB, when integrated into a library’s collection becomes cross-searchable with a potentially limitless array of other reference works. The price for e-books depends on the account type and population served. To register call (800) 877-4253 or e-mail gale.galeord@cengage.com.

In the Complete DSB new material is interleaved with old, but the actual material is not merged. Future emendations, additions, revisions, and updating will occur on a regular basis so that this standard reference source will remain definitive for many years to come. *George B. Kauffman, Department of Chemistry, California State University, Fresno, Fresno, CA 93740-8034, USA, georgek@csufresno.edu.*

It’s Part of What We Are: Some Irish Contributors to the Development of the Chemical and Physical Sciences, Science and Irish Culture Series No. 3. Charles Mollan, Royal Dublin Society, Ballsbridge, Dublin, Ireland, 2007; <http://rds.ie/science/publications>; to purchase or for additional information e-mail Dr. Claire Mulhall: science@rds.ie; hardbound, 2 vol., xlviii + 1770 pp, ISBN 978-0-86027-055-3, €60; €50 for RDS members (not including postage and packaging).

In 2004 the Royal Dublin Society initiated a series of volumes titled “Science and Irish Culture,” in which chemist Charles Mollan, a longtime member of the Royal Dublin Society (RDS) Committee of Science and Technology and an authority on the development of science in Ireland, played a prominent role. The first two volumes—D. Attis and C. Mollan, Ed., *Why the History of Science Matters in Ireland*, and C. Mollan, Ed., *Science and Ireland—Value for Society: A Volume to Acknowledge the Return to Dublin of the British Association for the Advancement of Science in September 2005*, appeared in 2004 and 2005, respectively. The third volume, the subject of this review, appeared in 2007.

Historians of Ireland have paid little attention to the role that men and women born in the Emerald Isle or with strong Irish connections, either at home or abroad, played in the advancement of science. For example, there is no university department devoted to the history of science in Ireland, whereas academic study of the history of science flourishes much more in countries outside of Ireland, especially in Great Britain and the United States, where scholars have taken a special interest in Ireland and Irish scientists. However, their studies have been scattered across the many books and journals dealing with the history of science in general or the history of specific sciences. Also, the Irish connections of scientists have often been ignored, particularly for those who emigrated to enjoy a more favorable environment than was available at home. Many of these scientists are claimed by their adopted countries, and their Irish background, which was of critical significance to their character and approach to their work, is overlooked. The series of RDS volumes specifically devoted to historical studies of Irish science and technology is intended to encourage a greater interest in this area by both scientists and historians. It may also have important lessons for other countries interested in

understanding how science relates to their culture, their society, and their opportunities for development.

It's Part of What We Are contains carefully researched and meticulously documented biographies, chronologically arranged according to birthdates and ranging in length from three pages to several dozen pages, profiling 118 astronomers, chemists, physicists, mathematicians, and other persons who played significant roles in advancing knowledge of the physical sciences during the last three centuries.

Mollan has left no stone unturned in his goal of focusing attention on the lives and achievements of these persons, whom he considers as people, not merely as scientists. He describes them “warts and all” and places them in the context of Irish—and to a lesser degree, international—scientific, social, educational, and political history. He deals not only with their scientific achievements but also with their views on other matters, often in their own words. As he puts it, “I do try to make human the people whom I am profiling, and I try to avoid jargon and too much scientific detail” (p xxxv). Wherever relevant, he includes their membership of and commitment to the Protestant ascendancy (the political, economic, and social domination of Ireland by great landowners, establishment clergy, and professionals, all members of the Established Church during the seventeenth through nineteenth centuries) and/or part in the struggle for Irish national independence.

Mollan also includes several exiled scientists, some of whom remained abroad for the remainder of their lives to the advantage of their adopted countries, while others returned home when conditions permitted. He explores their religious convictions, their scientific philosophy, and their views on the best forms for the education of Irish people of different persuasions over the relevant centuries. Although some of the persons profiled benefited from inherited wealth, e.g., the Boyles, most of the scientists came from ordinary middle class families. Largely overlooked in Irish historical studies, these persons exhibited remarkable abilities and accomplishments at a time when little encouragement for scientific endeavor existed in Ireland.

In this set, intended for a nonscientific readership, Mollan eschews technical terms and avoids chemical and mathematical equations so that readers with little knowledge of science can understand and enjoy the biographies. He includes numerous stories and anecdotes, both humorous and otherwise, as well as poetry, songs,

and other literary excerpts. His viewpoint is usually Irish (He repeatedly uses the phrase “this island”). His definition of “Irish” is extremely broad, and he includes persons who were born in Ireland but carried out their work elsewhere. He also includes two persons who, while not born in Ireland and whose major work was not performed there, had an Irish parent or parents—Joseph Black and Guglielmo Marconi.

“Labor of love” is often an overused expression, but in this case the appellation is fully justified. Mollan is obviously enjoying himself in spinning the tales that he relates. His style and tone are decidedly personal and conversational, and much of his writing is in the first person. Often he sprinkles his biographies with general observations or with revelations about himself so that we learn much about his life and career as well as that of his biographies.

For example, Mollan begins his essay on Aeneas Coffey (1780-1852), inventor of the Coffey still with the confession, “I am not a big drinker. I do, though, make my own wine, which we drink most evenings with dinner” (p 329). In his essay on George Boole (1815-1864) he acknowledges, concerning a biography of Boole, “I got my copy free (£19.95 was a serious amount of money to me in those days), since I had the pleasure of reviewing it for the *Irish Times* of 20 April 1985)” (p 734). (As a frequent book reviewer I can certainly empathize with him). His introduction to the essay on Hugh Ryan (1873-1931) shows his sly sense of humor: “It is interesting to speculate about the differences in personalities between those enlightened people, like me, who choose chemistry as their scientific specialisation, and those misguided souls who choose physics” (p 1,390). In another essay he states, “John Lighton Synge was one of the few people in this book whom I actually met” (p 1,511).

The set contains an “eclectic selection” of 149 illustrations of formal and informal single and group portraits, apparatus, telescopes, medals, title pages, advertisements, laboratories, buildings, caricatures, inventions, tombstones, newspaper articles, banknotes, and space groups from Mollan’s personal collection, reproduced on heavy, glossy paper in the middle of the two volumes (Fig. 1-76 between pp 406 and 407 in Vol. 1 and Fig. 77-149 between pp 1290 and 1291 in Vol. 2). References appear in abbreviated form at the bottom of each page and refer to the 78-page bibliography of books and articles in Vol. 2. A detailed index comprising 62 triple-column pages facilitates location of material. British spelling is used consistently throughout the set.

Mollan proclaims his goal and the set's title: "I hope that this book will confirm that we as a race have a tradition of innovation and that ability in the physical sciences is, indeed, Part of What We Are (p xli). In my opinion, he has succeeded in attaining his objective, and I am pleased to recommend this unique, scholarly but eminently readable, copiously illustrated, and modestly priced two-volume set to historians of science in general

and of Irish scientists in particular. It should also find a welcome home in academic and public libraries. As the most comprehensive treatment of the subject, hitherto never adequately addressed by a single author, it adds a previously undervalued dimension of what constitutes Irish culture. *George B. Kauffman, Department of Chemistry, California State University, Fresno, Fresno, CA 93740-8034, USA, georgek@csufresno.edu.*

Molecules that Changed the World. K.C. Nicolaou and T. Montagnon, John Wiley & Sons, Inc., New York, 2008, xvi + 385 pp, ISBN 978-3-527-30983-2, \$55.

The book by Nicolaou and Montagnon contains a fascinating description of science evolution through the discovery, identification, and development of individual molecules. Emphasis is placed on natural products with medicinal applications, and not unexpectedly, with a strong tie to the molecules of interest to the authors. It would be a faulty and naive assumption to believe that this book, or any book, could describe all of the molecules that 'changed the world;' and the authors go to great lengths to disavow themselves from that claim. Heavy emphasis is placed on the role organic chemists played in the development of each molecule; yet the book does not dwell on a detailed description of organic synthesis. Interplay between natural product science, biology, biochemistry, clinical data, and organic chemistry is highlighted. Scientific development, stimulated by these molecules, is revealed as a multidimensional equation that relies upon serendipity, dedication, and intellectual flash points.

A unifying feature of all chapters, with the exception of the chapter on Small Molecule Drugs, is the identification of a natural product as the impetus for the discovery and development. In this way the book makes a strong case for continued natural product discovery efforts and the role organic synthesis can play in understanding the natural product-medicine relationship.

The early chapters of the book are devoted to relatively simple molecules like urea, camphor, and aspirin; and the complexity of molecules of interest increases as one progresses through the book. Each chapter is organized in a similar fashion. The natural medicinal value of an unrefined natural product or the serendipitous discovery of a uniquely exciting substance is presented in the context of scientific advancement. The challenges encountered in taking advantage of these great opportunities are presented, with advances often tied to the efforts of synthetic organic chemists. Unlike *Classics in Total Synthesis*, detailed analyses of the synthetic pathways are modest and deemphasized, although references are provided for those readers interested in more of the synthetic details. The book is remarkably free of errors; and the appearance of low-technical mini reviews of topics like aldol reactions, asymmetric synthesis, metathesis reactions, and cross-coupling reactions will be useful for the non-expert. The final two chapters of the book are focused more directly on medical applications and provide a broad overview of pharmaceutical and biotechnology development.

The book is blessed with an abundance of beautiful illustrations and photographs. The style and quality of the graphical presentation are reminiscent of a National Geographic book. Many of the photographs are of individual scientists responsible for the scientific advances. While the organization of the book is based upon molecules, the individual scientist is the protagonist of each story. Personalities of the scientists who drove the discoveries are frequently revealed, often through the inclusion of quotations. The single-minded dedication of these scientists is celebrated, and their passion for discovery is placed front and center.

This book is targeted for a broad audience, and it will find use in a variety of constituencies. For the synthetic organic chemist, the book provides an opportunity to observe the beauty and innovation of synthetic approaches, as well as to appreciate the maturation of organic synthesis as a discipline. For the educator, the book will serve as a powerful resource for stories that can awaken sleepy undergraduates to the history of science and to

the possibilities that await the scientists of tomorrow. A reader with a modest familiarity with organic chemistry will appreciate, in addition to the history of individual molecules, the stories about individual scientists, whose dedication, passion, and insight moved chemistry and, in many cases, all of science forward. *Charles K. Zercher, University of New Hampshire, Durham, NH 03824.*

Nylon and Bombs: DuPont and the March of Modern America. Pap A. Ndiaye, translated by Elborg Forster, Johns Hopkins University Press, Baltimore, MD, 2007, ISBN 978-0-8018-8444-3, hardcover, \$45.

This is a very important book that ought to be read by all chemical engineers who seek a broad understanding of the history of their profession. The author brings to bear on this history an impressive collection of analytical and descriptive tools and a carefully designed and clearly articulated understanding of the context of the development of chemical engineering that produces a masterpiece. The original appeared in 2001, written in French from Ndiaye's professorial post at the École des Hautes Études en Sciences Sociales (the school of advanced social science) in Paris. It has been ably rendered in English by Elborg Forster.

The author has chosen to focus on MIT and the DuPont Company, both of which are exemplary, leading academic and educational institutions in the field. While the AIChE plays a role in catalyzing the development of the profession in this account, it is not the central agency, as it is in most accounts of the profession. Instead, the crucial interactions between MIT and DuPont produced many of the curricular and research innovations that shaped the status and success of chemical engineers in the 20th century.

While this focus excludes developments in petrochemicals, in which DuPont had little interest, it takes advantage of the abundant evidence available at the Hagley Library and Archives, one of the few significant industrial chemistry archives open to outsiders. Ndiaye

also uses interviews with DuPont engineers as well as a wide range of secondary sources, which are conveniently evaluated in an appended historiographical essay.

The author's solid grounding in American history allows him to describe this interaction between DuPont and MIT in the political environment of the 20th century. The political relations of DuPont and the federal government in the Progressive Era and the New Deal were difficult. As the largest manufacturer of explosives before and during World War I, the firm came under the scrutiny of both Theodore and Franklin Roosevelt's administrations, as well as the United States Congress, most notably the Nye Committee, to whom the firm appeared to be a "Merchant of Death" in World War I. World War II reconciled the firm with the federal government, which needed its expertise in both traditional and nuclear explosives.

One response of the company to a hostile political environment was to diversify its product line after World War I. The opportunity was presented by the seizure of German chemical patents by the Alien Property Custodian during that war, which allowed chemical firms in the United States to contemplate competition with Germany in synthetic chemistry. One product of this contemplation was nylon, DuPont's signature contribution to both military and consumer markets after 1939.

The diversification under Pierre S. du Pont brought the company into collaboration with MIT, where A. D. Little, William Walker, and Walter Lewis, the canonical founders of the discipline of chemical engineering, had created the most prominent department in the field just after the war. Since Pierre and other du Ponts were alumni of the Institute, it was a "natural" choice for an

academic partner; but the negotiations between the Institute and DuPont were complicated by their academic and industrial cultures. The nuances of these negotiations are deftly described by Ndiaye, who points out that chemical engineers had to struggle for recognition and respect from the chemists, who dominated both the MIT Chemistry Department and the DuPont Wilmington Experimental Station. His parallels between academic and corporate politics illuminate barriers that stood in the way of the social and professional aspirations of chemical engineers in the 1920s and 1930s.

The protagonists of the story are the chemical engineers who joined DuPont after World War II and established their value to the firm in the development of nylon in the 1930s. Crawford Greenewalt stood out among them, both because of his elite background (he was related by marriage to the du Pont family) and because of his extraordinary ability to embrace the culture of the Wilmington firm. Within a quarter of a century, he rose to the presidency, solving the production problems posed by scaling up Wallace Carother's novel polymer, nylon, and the complexities of mass-producing Glenn Seaborg's novel element, plutonium. Using Greenewalt as the most prominent representative of DuPont's chemical engineers, Ndiaye is able to depict the personal, professional, and political dimensions of their rise to leadership in the firm, their success in both the commercial and military markets, and their role in reshaping the corporate culture of DuPont.

The technical aspects of nylon and plutonium production are less developed in this account. Although nylon has been the subject of considerable interest by other historians of DuPont, particularly in David Hounshel and John Smith's history of DuPont research and development, it is beyond the institutional and historical focus of the account presented here. Such technical accounts of the development of plutonium are fewer in number and, in the current climate of concern over nonproliferation, unlikely to be widely available soon. Nevertheless, published accounts by Seaborg and newly available notes by Greenewalt might have afforded some explanation of the challenges DuPont faced. The author's reliance on the official histories of the Atomic Energy Commission, dating back almost fifty years, rather than on more recent accounts, makes this part of his narrative less satisfying.

Nevertheless, the "big picture" of nylon and bomb production presented here is limned with analyses that seldom appear in more restricted accounts of these two new signature materials. These analyses are explicit and buttressed with convincing research and state-of-the-art historical methodology. Since historians of technology have largely escaped the prolixity in their terminology, the book is easily accessible to the laity and well worth reading. *Robert W. Seidel, Department of Chemical Engineering and Materials Science, University of Minnesota, Minneapolis, MN 55455.*

Distilling Knowledge: Alchemy, Chemistry, and the Scientific Revolution. Bruce T. Moran, Harvard University Press, Cambridge, MA, 2005, hardcover, 210 pp, ISBN 0-674-01495-2, \$16.95.

Andreas Libavius and the Transformation of Alchemy. Bruce T. Moran, Watson Publishing International LLC, Sagamore Beach, CA, 2007, hardcover, vii + 344 pp, ISBN 978-0-88135-395-2, \$49.95.

Within the 16th and 17th centuries, the history of alchemy and chemistry can seem a murky place. Alchemy seemed to be moving away from the traditional pursuit

of the transmutation of metals and began focusing more and more on preparation of medicines. At the same time, chemistry itself was not yet a distinct practice or discipline, and individuals commonly pursued both "alchemical" and "chemical" activities without significant distinction. To further complicate the study of this time period, even the terms "alchemy" and "chemistry" were used largely interchangeably making it nearly impossible to separate these two fully intertwined practices. In recognition of this difficulty, the pivotal work of Newman and Principe has advocated the use of the archaically-spelled term chymistry to refer to the activities of this time period, as they can not be purely differentiated into either chemistry or alchemy. It is into this murky, yet rich, time

period that historian Bruce T. Moran delves with two texts covering the transition of alchemy to chemistry.

In the first of these publications, *Distilling Knowledge: Alchemy, Chemistry, and the Scientific Revolution* (2005), Moran argues the important contribution of alchemy to the Scientific Revolution and proposes that, rather than the common perception of alchemy as irrational and pseudoscientific, it should be considered an early form of scientific pursuit when viewed within the context of the time period and cultural perspective. Most historians of chemistry recognize the contributions of alchemy to the development of chemistry, particularly in terms of techniques (distillation, sublimation, etc.), laboratory apparatus (stills, heating baths, flasks, etc.), and the isolation of important chemical species (alcohol, inorganic salts, mineral acids, etc.). Moran highlights many of these contributions. The arguments put forth for the scientific nature of alchemy, however, suffer from the fact that Moran seems to ignore the complications of distinguishing chemistry from alchemy as discussed above, and he offers what could be viewed as the more "chemical" activities of practitioners as the strongest evidence of the "scientific" contributions of alchemy. At points, he does acknowledge that some authors used the term chemistry to refer to alchemy but seems to suggest that these are purely alchemical activities. Another confusing aspect of Moran's presentation is that he often seems to equate discovery or technology with science. Processes and practices are stressed to be as important to the pursuit of knowledge as theory, but he does not seem to acknowledge that process and practice alone can not advance understanding. However, it should be pointed out that while the contributions of alchemy may have been primarily practical, it was practitioners' interest in these techniques and the materials produced from them that ultimately led to the development of chemistry. Thus, the important contributions of alchemy in the history of science should not be overlooked; and in advocating these contributions, Moran is definitely passionate.

Overall, it is unclear as to who was the intended audience of this book. The writing style and discussion, particularly early in the text, seem to suggest the book was written for a general audience, but the overall discussion requires at least some knowledge of the subject. For example, while a large number of examples of the

activities of various alchemists are provided, it is never explained what it is that defined alchemy as an activity prior to its intermingling with the beginnings of chemistry, nor does it give background into the underlying theories on which alchemy was based. Likewise, familiarity with the general ideas and work of Hippocrates, Galen, and Aristotle is assumed. As such, this book is not a good starting point for those interested in the later alchemical era, but neither does it really offer enough new material or insight to provide significant interest to more knowledgeable readers.

Moran's second offering came two years later with *Andreas Libavius and the Transformation of Alchemy* (2007), a study of the life, writings, and philosophy of German alchemist Andreas Libau (ca.1560-1616), more commonly known through the Latinized name Libavius. While it covers some of the same ground as his previous text, this work is drastically different in nature and is clearly an academic text aimed at the historian of chemistry. The discussion is logically presented and well written, with each chapter heavily footnoted with sources and further comment. In addition, the general confusion of alchemy vs. chemistry seen in the previous work has been replaced with the use of chymistry as advocated by Newman and Principe, although it should be noted that Moran's use of the word is more of a pre-chemistry and, at times, he still tries to differentiate it from 16th-century alchemy.

Libavius is most well known for his work *Alchemia* (1597), which is considered by some to be the first systematic textbook on chymistry. Moran, however, does not limit himself to this single work and presents material from a fair number of lesser known writings as well. Moran focuses on the general philosophy of Libavius, presenting his views on the place and nature of chymistry, while also describing many of Libavius' various conflicts with supporters of Paracelsian doctrine. With the exception of a brief description of Libavius' design for a model laboratory, the technical aspects of Libavius' writings are not discussed. But even with this limitation, Moran presents plenty of interesting material and provides a deeper look at this important historical figure. Overall, this book is a worthy addition to the collection for those studying this complicated period of the history of chemistry. *Seth C. Rasmussen, North Dakota State University.*

Nobel Laureate Contributions to 20th Century Chemistry. David Rogers, Royal Society of Chemistry, Cambridge, 2006, xii + 651 pp, ISBN 0-85404-356-X, £99.95.

Rogers has assembled biographical information and descriptions of Nobel laureates' scientific innovations from 1901 to 2000 in this invaluable reference source. As the title indicates, these laureates made contributions to chemistry, although they were not always recipients of the Nobel Prize in Chemistry. Hence, Rogers has included, in a separate section, recipients of the Nobel in Physiology or Medicine, but whose research was substantially chemical in nature.

A brief preface allows the author to explain his reason for undertaking this ambitious project and to comment on a few outstanding examples of laureates: Marie Curie, the only woman to have received two awards; Linus Pauling, who uniquely was awarded two undivided Nobel Prizes; Fred Sanger, the only recipient of two Nobel Prizes in Chemistry.

There follows a short section on Alfred Bernhard Nobel, the benefactor and creator of the idea of these prizes, which includes a quotation from his will spelling out the guidelines for the award program.

Section 1, "Chemists Awarded the Nobel Prize for Physiology or Medicine," 22 pages in length, begins with

Henrik Carl Peter Dam, 1943, and concludes with Martin Rodbell, 1994. The major portion of the book, Section 2, with 615 pages, covers all the chemistry Nobel Prize winners from 1901 to 2000.

Four to five pages are allotted to each awardee, whose picture is followed by biographical information "The Early Years," "The Career," "Honors and Awards," and with a fairly detailed account of the research accomplishments. A bibliography is included for each biography. Those laureates who shared a prize are so designated as "0.5," "0.33," or "0.25."

As the author laments, many are called but few are chosen. He offers recognition of those who were nominated (up through 1950) but never elected in a table in Section 3, "Collaborations and Influences." A sampling of those with fervent but unheeded support are G. N. Lewis (nominated 17 years); Lisa Meitner (nominated 14 years); and Georges Urbain (nominated 22 years)! Also in Section 3 are tabular and graphical analyses and professional "family trees," to illustrate the interconnection between Nobel Prize winners. Finally, the index is a cumulative alphabetical listing of Nobel laureates from Sections 2 and 3.

All chemists with even the least enthusiasm for the history of their discipline will find this compendium of enormous value and will treasure owning it. *Paul R. Jones, University of Michigan.*

CALL FOR NOMINATIONS FOR THE 2009 EDELSTEIN AWARD

The Division of History of Chemistry (HIST) of the American Chemical Society (ACS) solicits nominations for the 2009 Sidney M. Edelstein Award for Outstanding Achievement in the History of Chemistry. This award, first given in 2002, honors the memory of the late Sidney M. Edelstein, who established the Dexter Award in 1956, and continues the tradition of the Dexter Award for Outstanding Achievements in the History of Chemistry, which was discontinued after 2001. Lists of previous recipients of the Edelstein Award and its predecessor Dexter Award are available at the HIST webpage (<http://www.scs.uiuc.edu/~mainzv/HIST/>).

The Edelstein Award is sponsored by Ruth Edelstein Barish and family and is administered by HIST. The recipient chosen to receive the Edelstein Award is presented with an engraved plaque and the sum of \$3500, usually at a symposium honoring the recipient at the Fall National Meeting of the ACS. The award is international in scope, and nominations are welcome from anywhere in the world. Previous winners of the Dexter and Edelstein Awards include chemists and historians from the United States, Canada, Germany, France, the Netherlands, Hungary, Israel, and the United Kingdom.

A complete nomination consists of

- a complete curriculum vitae for the nominee, including biographical data, educational background, awards, honors, list of publications, and other service to the profession;
- a letter of nomination summarizing the nominee's achievements in the field of history of chemistry and citing unique contributions that merit a major award; and
- at least two seconding letters.

Copies of no more than three publications may also be included. Only complete nominations will be considered for the award.

All nomination materials should be submitted in triplicate to Anthony S. Travis, Chair of the Edelstein Award Committee for 2009, Edelstein Center, Safra Campus, The Hebrew University of Jerusalem, Givat Ram, Jerusalem 91904, Israel (email: travis@cc.huji.ac.il) for arrival no later than December 31, 2008.

INSTRUCTIONS FOR AUTHORS

Articles usually of 4-12 pages, typed, double-spaced (excluding references) are to be submitted electronically, in MS Word or WordPerfect as an email attachment, to **Editor, Bulletin for the History of Chemistry**, at the University of Michigan at prjones@umich.edu.

All images including photos, illustrations, graphs and chemical formulas should be submitted as separate tif, jpg or eps files at 300 dpi, actual printing size. You may indicate image placement in the document with a brief text notation. Do NOT imbed images in the manuscript. Include captions at the end of the manuscript.

The title of the article should be of reasonable length (up to 15 words); a subtitle may be included if appropriate. Authors should strive to make the title descriptive of the specific scope and content of the paper, bearing in mind that the title will determine entries in the subject index. Subheadings within the paper may be used if authors feel their inclusion will enhance clarity.

Manuscript titles should be in all caps. Paragraphs should be in block style (no indent). Direct quotations should be in block style also.

REFERENCES AND NOTES should appear at the end as part of the main document and not buried as footnotes. In the main text, references are identified by Arabic numbers within parentheses—**no superscripts**.

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1. O. T. Benfey, "Dimensional Analysis of Chemical Laws and Theories," *J. Chem. Educ.*, **1957**, 34, 286-288.
2. G. W. Wheland, *Advanced Organic Chemistry*, Wiley, New York, 1949.
3. J. R. Partington, *A History of Chemistry*, Macmillan, London, 1972, Vol. 4, 104-105.
4. Ref. 3, 1962, Vol. 3, p 763.
5. L. P. Rowland, Ed., *Merritt's Textbook of Neurology*, 8th ed., Lea and Febiger, Philadelphia, PA, 1989.
6. K. A. Nier, The Emergence of Physics in Nineteenth-Century Britain as a Socially Organized Category of Knowledge. Preliminary Studies, Ph.D. Thesis, Harvard University, 1975.
7. J. B. Conant, "Elmer Peter Kohler," *Biogr. Mem. Nat. Acad. Sci.*, **1952**, 27, 264-291.

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