

THE BECKMAN CENTER FOR THE HISTORY OF CHEMISTRY

LEO H. STERNBACH

Transcript of an Interview  
Conducted by

Tonja Koepfel

at

Hoffmann-La Roche Inc.  
Nutley, New Jersey

on

12 March 1986

THE BECKMAN CENTER FOR THE HISTORY OF CHEMISTRY  
Oral History Program

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*Leo H. Sternbach*

Dr. Leo H. Sternbach

(Date)

*June 17, 1991*

LEO H. STERNBACH

1908 Born in Abbazia, Austria on 7 May

Education

University of Cracow  
1929 M. Pharmacy  
1931 Ph.D., organic chemistry  
1931-1937 Research Assistant with Professor K. Dziewonski  
1937-1940 Research Fellow with Professor L. Ruzicka,  
Eidgenössische Technische Hochschule, Zürich

Professional Experience

1940-1941 Research Chemist, Hoffmann-La Roche, Basel,  
Switzerland  
Hoffmann-La Roche, Nutley, New Jersey  
1941-1959 Group Chief  
1959-1965 Senior Group Chief  
1965-1967 Section Chief  
1966-1973 Director of Medicinal Chemistry  
1973- Consultant

Honors

1971 Honorary Dr. of Technical Sciences, Technical  
University, Vienna, Austria  
1977 Outstanding Naturalized Citizen Award, Newark  
Chapter, Unico National  
1978 Medicinal Chemistry Award, American Chemical  
Society, Division of Medicinal Chemistry  
1979 Cecil Brown Lectureship, American Chemical Society,  
North Jersey Section  
1979 Award for Creative Invention, American Chemical  
Society  
1979 Chemical Pioneer Award, American Institute of  
Chemists  
1982 John Scott Medal Award, Board of Directors of City  
Trusts, Philadelphia, Pennsylvania  
1984 Charles W. Hartman Memorial Lecture, University of  
Mississippi  
1984 Honorary Doctor of Science, Centenary College,  
Hackettstown, New Jersey  
1984 Carl-Mannich-Medal, German Pharmaceutical Society  
1986 Honorary Dr. phil. nat. h.c., Johann Wolfgang  
Goethe-Universität, Frankfurt am Main

## ABSTRACT

Leo H. Sternbach begins the interview with a discussion of his family and childhood in Austria and Poland. He describes his early education during the First World War as well as his experiences working in his father's pharmacy. After receiving a degree in pharmacy from Jagiellonian University in Cracow, he enrolled in a Ph.D. program in organic chemistry. As a result of intensifying anti-Semitism, he left Poland and went to Vienna, where he worked with Pauli and Fränkel, and then to Zürich to work with Ruzicka at the Swiss Federal Institute. After beginning work with Hoffmann-La Roche in Basel and marrying Herta Kreuzer, increasing pressure to leave Switzerland compelled him to emigrate to the United States, where he continued work with the company in Nutley, New Jersey and began a search for new tranquilizers. Sternbach recalls that he was instructed to terminate his study of benzodiazepines but continued the research unofficially, which led to his significant discoveries of Librium, Valium, and other related drugs. He concludes the interview with a brief summary of his accomplishments and his views on the present state of pharmaceutical research.

## INTERVIEWER

Dr. Tonja A. Koepfel received a master's degree in chemistry from the Swiss Federal Institute of Technology in 1944. Since then she has written about chemistry, done research, and taught college chemistry. Dr. Koepfel is also a historian of chemistry. In 1973 she earned a Ph.D. degree in the history and sociology of science from the University of Pennsylvania. She is especially interested in the development of organic chemistry in the nineteenth and early twentieth centuries.

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- 1 Childhood  
Born 7 May 1908 in Abazzia, Austria. Multinational, multilingual family. Works in father's pharmacy. Attends elementary school during World War I. Italy occupies Abazzia during Gymnasium years. Moves to Villach where strong interest in chemistry develops. Uses window sill for laboratory. Parents return to Poland; completes Gymnasium there.
- 7 Jagiellonian University in Cracow  
Enrolls in pharmacy curriculum, including several chemistry courses. Ph.D. program in organic chemistry with Professor Dziejowski. Thesis on thioindigo dyes. Loves crystallization. Laboratory conditions. Post doctoral study on aromatic amines, pyrene and Friedel-Crafts reactions. Future prospects at university poor, urged to leave, because Jewish.
- 12 Eeliks Wislicki Foundation  
Receives grant to work with (elder) Pauli in Vienna. Works on conductivity determinations, but real interest is organic chemistry. Goes to Fränkel part time for organic work but laboratory conditions and experiments in progress disappointing.
- 14 Swiss Federal Institute of Technology (ETH)  
Research fellow under Ruzicka in Zürich. Studies diterpenes. Meets future wife. Enjoys skiing. Close relationship with Ruzicka.
- 19 Hoffmann-La Roche  
Moves to Basel. Marries Herta Kreuzer. "Encouraged" to leave Switzerland. Emigrates to United States. Senior Chemist in Nutley, New Jersey. Works on syntheses of riboflavin, dosable arsenicals, biotin, biotinol. Seven patents in biotin field with Goldberg. Begins work with 1,4-benzodiazepines in search for new tranquilizers. Stops this work under Goldberg's instructions, but continues unofficially with Reeder while working on antibiotics. Success allows to resume official research on benzodiazepines, leading to discoveries of Librium, Valium, and other related tranquilizers and hypnotics. Discussion of animal testing. Effects of Valium. Sells patents to Hoffmann-La Roche with no regrets.
- 36 Leisure Activities  
Enjoys skiing, travel. Frequent trips to Switzerland. Son also a chemist.

39	Awards and Honors
	American Chemical Society Awards. Honorary doctorates. John Scott Medal. Numerous publications, discoveries, and patents.
42	Notes
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## NOTES

A complete list of the publications and patents of Leo Sternbach may be found in the Beckman Center Oral History File #0043.

1. K. Dziewonski, C. Baraniecki, and L. H. Sternbach, "A New Method for the Preparation of Thioindigo Dyes. I. Syntheses in the Naphthalene Group," Bulletin International de l'Academie Polonaise des Sciences et des Lettres, Classe des Mathematiques et Naturelles, Series A: Sciences Mathematiques, (1930A): 198-202.
2. K. Dziewonski and L. H. Sternbach, "The Reaction Between Benzoyl Chloride and alpha-Naphthylamine," Bulletin International de l'Academie Polonaise des Sciences et des Lettres, Classes des Mathematiques et Naturelles, Series A: Sciences Mathematiques, (1935A): 327-332; K. Dziewonski and L. H. Sternbach, "Pyrene," Roczniki Chemii, 17 (1937): 101-104.
3. Wo. Pauli and L. H. Sternbach, "Comparative Electrochemical Studies of Highly Purified Lyophilic Sols. VI. Electrochemistry of Sols of Alginic Acid," Kolloid-Zeitschrift, 84 (1938): 291-303.
4. Sigmund Frankel, Die Arzneimittel Synthese (Berlin: Julius Springer Verlag, 1927).
5. Wo. Pauli and L. H. Sternbach, "Electrochemistry of the Agar Sol," Helvetica Chimica Acta, 24 (1941): 317-339.
6. L. Ruzicka and L. H. Sternbach, "Diterpenes. XXXIV. Origin and Degradation of Tetrahydroxyabiatic Acid," Helvetica Chimica Acta, 21 (1938): 565-583.
7. M. W. Goldberg and L. H. Sternbach, "Synthesis of Biotin," U.S. Patent 2,489,232, issued 22 November 1949 (application filed 31 May 1946); Goldberg and Sternbach, "Synthesis of Biotin," U.S. Patent 2,489,235, issued 22 November 1949 (application filed 24 July 1947).
8. M. W. Goldberg and L. H. Sternbach, "Imidazolido-tetrahydrofurans," U.S. Patent 2,489,233 issued 22 November 1949 (application filed 26 April 1947); Goldberg and Sternbach, "Thiophanes and the Method for Their Production," U.S. Patent 2,489,234 issued 22 November 1949 (application filed 16 July 1947); Goldberg and Sternbach, "Synthesis of Biotin and Related Compounds," U.S. Patent 2,489,236 issued 22 November 1949 (application filed 24 July 1947); Goldberg and Sternbach, "3,4-(2'-Keto-Imidazolido)-2- -hydroxy-pentyl-thiophanes," U.S. Patent 2,489,237 issued 22 November 1949 (application filed 8 June 1948); Goldberg and Sternbach, "Debenzylation of Benzylated

Imidazolido-thiophane Compounds," U.S. Patent 2,489,238 issued 22 November 1949 (application filed 8 June 1948); see also note 7.

9. L. H. Sternbach, The Benzodiazepine Story (Basle, Switzerland: F. Hoffman-La Roche & Co., 1980; second edition 1983).
10. L. H. Sternbach and E. Reeder, "Quinazolines and 1,4-Benzodiazepines. II. The Rearrangement of 6-Chloro-2-chloromethyl-4-phenylquinazoline 3-Oxide into 2-Amino Derivatives of 7-Chloro-5-phenyl-3H-1,4-benzodiazepine 4-Oxide," Journal of Organic Chemistry, 26 (1961): 1111-1118.
11. E. Reeder and L. H. Sternbach, "Quinazolines and 1,4-Benzodiazepines. IV. Transformations of 7-Chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-Oxide," Journal of Organic Chemistry, 26 (1961): 4936-4941.
12. L. Shearer, "The Man Who Invented Valium," Parade, (27 June 1976): 8-10.
13. E. Reeder and L. H. Sternbach, "5-Aryl-3H-1,4-Benzodiazepin-2(1H)-Ones," U.S. Patent 3,371,085, issued 27 February 1968 (application filed 10 December 1959).



## INDEX

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A few important chronological data in the development of Ro 5-0690

- May 7, 1957      Submitted for pharmacological testing.  
Data sheet.
- July 26, 1957    Pharmacological activity reported by Dr. Randall  
and Mrs. Kappell, RCR #11788.
- Sept. 24, 1957   Discussed at Advisory Group to Research Steering  
Committee. Shift planned from hydrochloride to  
more stable base for toxicity and ultimately  
clinical testing.

March 19, 1958 I.O. Dr. Bagdon to Dr. Randall. Comparison of toxicity to R0 5-0690 with Ro 5-0690/1 (free base). Hydrochloride R0 5-0690 less toxic. Base caused local intestinal irritation.

April 15, 1958 Structural proof reported by Sternbach in RCR #4328.

April 25, 1958 Analytical Data Sheet Dr. Wollish RCR #12308.

April 30, 1948 Preliminary Pharmacology Data Sheet Dr. Randall RCR #12189.

May 15, 1958 Patent application filed for 1,4-Benzodizepine 4-Oxides.

June 5, 1958 Clinical Data Sheet, S. R. Gustafson RCR # 12677.

June 18, 1958 Preliminary clinical studies started under Dr. Chapman.

Dec. 22, 1958 1-year chronic toxicity studies started by Dr. Bagdon.

July 7, 1959 Intensive clinical studies started by Dr. Hines near end of 1958. Patent issued.

September 1959 Princeton meeting.

November 1959 Galveston meeting.

February 1960 Introduced.

April 8, 1960 Luncheon.

April 1961 Chemical paper. Submitted April 1960.

July 7, 1976 Patent expires.

First pharmacology activity 1957, introduced February 1960 - 2 1/2 years.



Valium

Oct. 26, 1959 First made with diazomethane. RN 161.  
Nov. 27, 1959 Chemical Data sheet. Analysis Nov. 16. 2046.  
Dec. 10, 1959 Patent application.

1. Animal tolerance studies authorized - see RSC No. 1/60  
Dated January 7, 1960. started Feb. 10, 1960.
2. Long Term Chronic Toxicity Trials authorized February 11,  
1960 - see RSC No. 5/60.
3. Pharmacological data sheet May 3, 1960 - see Randall RCR  
14,308.
4. Given to Dr. Abrams May 10, 1960.
5. Preliminary clinical trials authorized May 12, 1960 - see  
RSC 15/60.
6. Chronic toxicity in dogs authorized September September 29,  
1960 - see RSC 33/60.
7. Clinical data sheet March 27, 1961 - Gustafson, Gordon -  
see RCR 11,245.
8. Dr. Bagdon RCR 14952, October 25, 1961.
9. NDA December 15, 1961.
10. Introduced December 1963.
11. Patent issued February 27, 1968, U.S. 3,371,085.

First tested November 1959, introduced December 1963 - over 4  
years.