

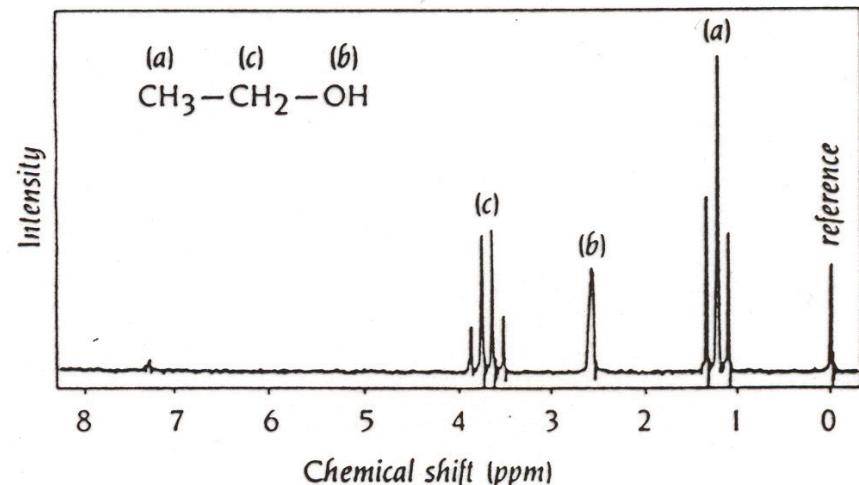
# NMR SPECTROSCOPY

## INTRO

# NMR: SOPHOMORE ORGANIC CHEMISTRY

- Sophomore organic NMR:

- 1D,  $^1\text{H}$  spectra
- small organic molecules
- one signal for each type of  $^1\text{H}$
- signals split into doublets, triplet, quartets, etc., due to presence of  $^1\text{H}$  nuclei on neighboring carbon atoms ("coupling")
- frequencies ("chemical shifts") of signals determined by electron density



- This course:

- what gives rise to the signals; microscopic and macroscopic
- what determines signal frequencies, intensities and multiplicities (chemical shifts/couplings/relaxation)
- how are spectra acquired and processed (pulsed Fourier transform methods)
- how can we manipulate nuclear magnetism to get other types of information (complex pulse sequences)
- 2D methods / chemical shift correlation (COSY, TOCSY)
- the nuclear Overhauser effect (NOE, NOESY)
- etc.

# NMR ACTIVE NUCLEI

- Most elements are comprised of one or more isotopes that are NMR active

1    2    3    4    5    6    7    8    9    10    11    12    13    14    15    16    17    18

<u>H</u>															<u>H</u>	<u>He</u>			
<u>Li</u>	<u>Be</u>													<u>B</u>	<u>C</u>	<u>N</u>	<u>O</u>	<u>F</u>	<u>Ne</u>
<u>Na</u>	<u>Mg</u>													<u>Al</u>	<u>Si</u>	<u>P</u>	<u>S</u>	<u>Cl</u>	<u>Ar</u>
<u>K</u>	<u>Ca</u>	<u>Sc</u>	<u>Ti</u>	<u>V</u>	<u>Cr</u>	<u>Mn</u>	<u>Fe</u>	<u>Co</u>	<u>Ni</u>	<u>Cu</u>	<u>Zn</u>	<u>Ga</u>	<u>Ge</u>	<u>As</u>	<u>Se</u>	<u>Br</u>	<u>Kr</u>		
<u>Rb</u>	<u>Sr</u>	<u>Y</u>	<u>Zr</u>	<u>Nb</u>	<u>Mo</u>	<u>Tc</u>	<u>Ru</u>	<u>Rh</u>	<u>Pd</u>	<u>Ag</u>	<u>Cd</u>	<u>In</u>	<u>Sn</u>	<u>Sb</u>	<u>Te</u>	<u>I</u>	<u>Xe</u>		
<u>Cs</u>	<u>Ba</u>	*	<u>Hf</u>	<u>Ta</u>	<u>W</u>	<u>Re</u>	<u>Os</u>	<u>Ir</u>	<u>Pt</u>	<u>Au</u>	<u>Hg</u>	<u>Tl</u>	<u>Pb</u>	<u>Bi</u>	<u>Po</u>	<u>At</u>	<u>Rn</u>		
Fr	Ra	**	Rf	Ha	Sg	Ns	Hs	Mt											

\*La Ce Pr Nd Pm Sm Eu Gd Tb Dy Ho Er Tm Yb Lu

\*\*Ac Th Pa U Np Pu Am Cm Bk Cf Es Fm Md No Lr

<http://bouman.chem.georgetown.edu/NMRpt/NMRPerTab.html>

## HISTORY\*

1940s	-First observation of nuclear magnetic resonance in solids and liquids (1945)
1950s	-Development of chemical shifts and spin-spin coupling constants as structural tools
1960s	-Superconducting magnets -Pulse Fourier transform approach developed -Nuclear Overhauser effect used for structure determination
1970s	-Computer control
1980s	-Development of multipulse and two dimensional techniques -Automation
1990s	-Pulsed field gradients -Coupled ("hyphenated") methods (i.e. LC-NMR)
2000-present	-High-sensitivity cryogenic probes -Very high fields (> 900 MHz)

\*From Claridge, "High-Resolution NMR Techniques in Organic Chemistry"

# RECOGNITION



- 1944 – Isidor Isaac Rabi - Nobel Prize in Physics
  - "for his resonance method for recording the magnetic properties of atomic nuclei"
- 1952 – Felix Bloch and Edward Mills Purcell – Nobel Prize in Physics
  - "for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"
- 1991 – Richard Ernst – Nobel Prize in Chemistry
  - "for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy"
- 2002 – Kurt Wuthrich – Nobel Prize in Chemistry
  - "for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution"
- 2003 – Paul Lauterbur and Sir Peter Mansfield – Nobel Prize in Physiology and Medicine
  - "for their discoveries concerning magnetic resonance imaging"

# HISTORY

First NMR signals (~ 1946)\*

- $^1\text{H}$  signal from  $\text{H}_2\text{O}$  at 7.76 MHz



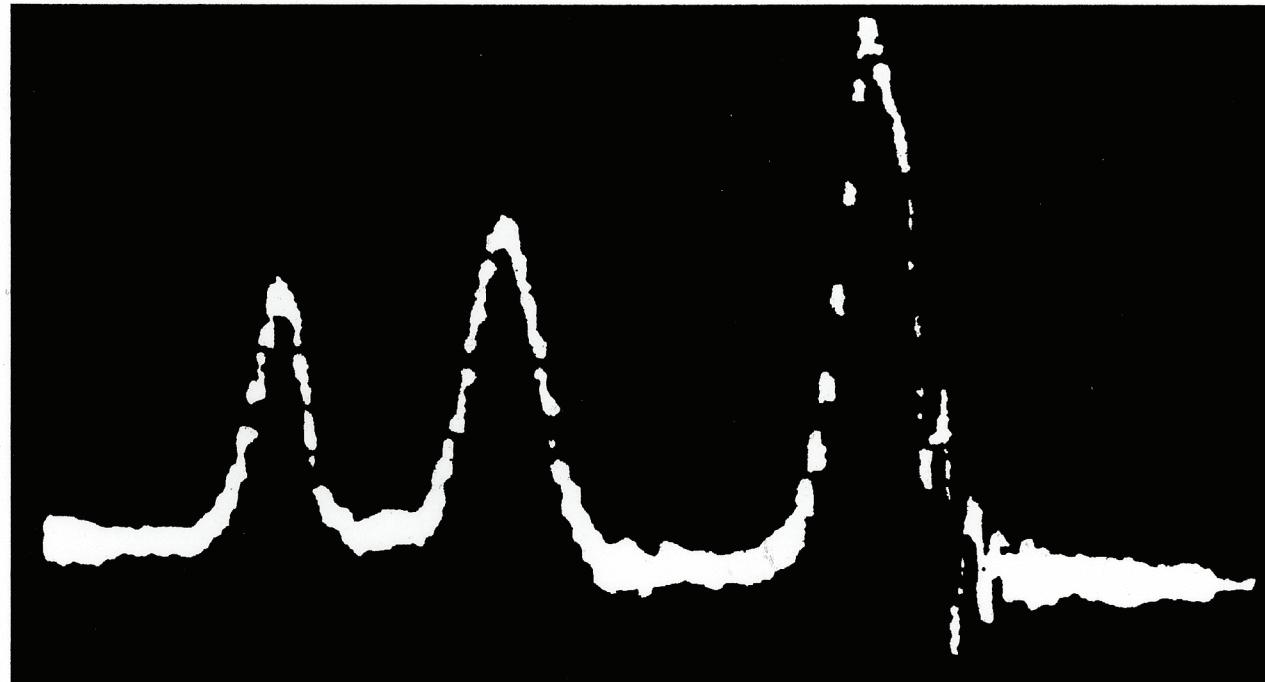
\*Bloch, F., Hansen, W. W., and Packard, M., (1946) **Nuclear Induction**. *Phys. Rev.* 69, 127.

\*Bloch, F., Hansen, W. W., and Packard, M. (1946) **The Nuclear Induction Experiment**. *Phys. Rev.* 70, 474-489.

## HISTORY

First published ‘high-resolution’  $^1\text{H}$  NMR spectrum (1951)\*

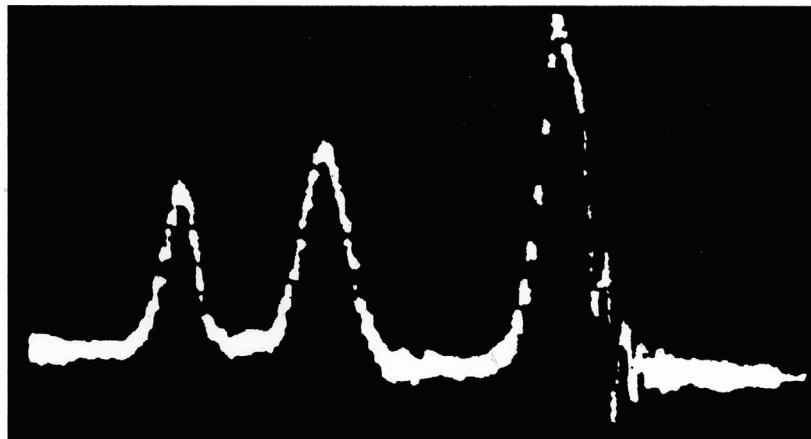
-spectrum of ethanol demonstrated that NMR spectra were a source of structural information (now, chemists got interested)



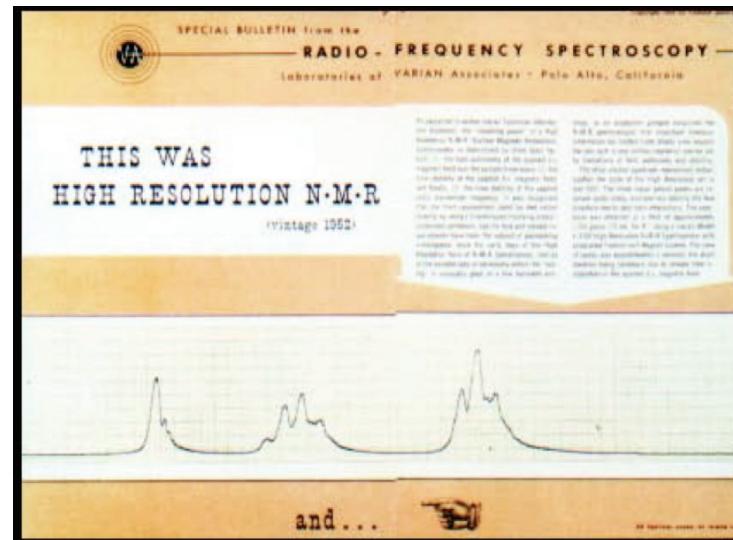
\*Arnold, J. T., Dharmatti, S. S., and Packard, M. E., (1951) **Chemical Effects on Nuclear Induction Signals from Organic Compounds.** *J. Chem. Phys.* **19**, 507.

# HISTORY

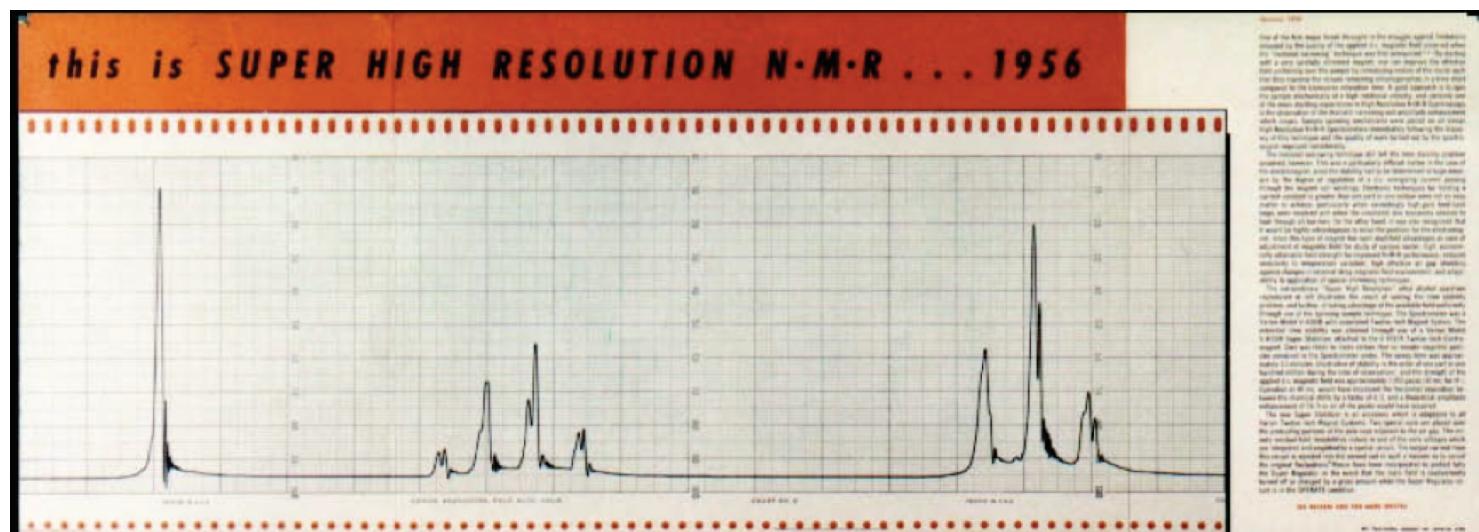
Ethanol - 1951



Ethanol - 1952



Ethanol - 1956

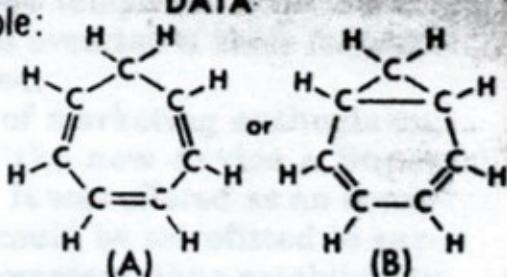
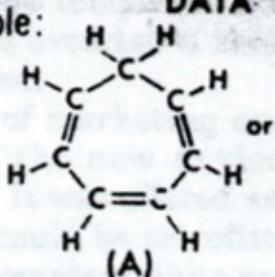
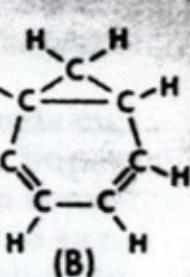


# HISTORY

The first chemical problem solved by NMR  
-signal integration discriminated between  
possible synthesis products

**20 USE OF INTEGRATED INTENSITIES IN STRUCTURE ANALYSIS**  
(Number 20 of a series)

**DATA**

Sample:   
(A)   
(B) 

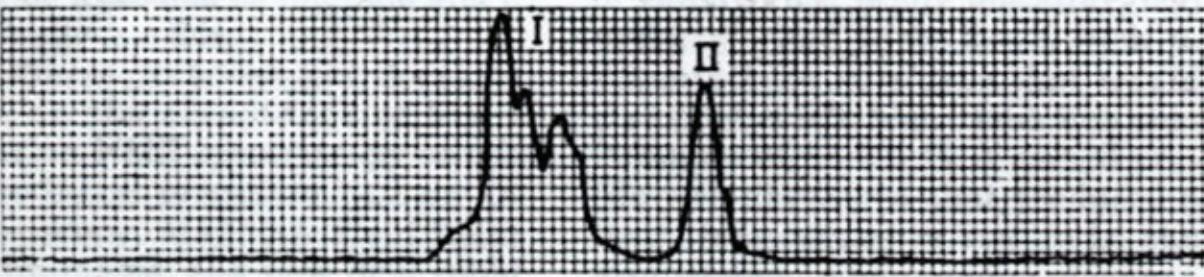
Volume: 0.01 cc.  
Signals Observed: H<sup>1</sup>  
Frequency: 30 mc.  
Field: 7050 gauss

**INTERPRETATION**

In solving the problem of whether structure A or B correctly represents the sample submitted for analysis, it becomes necessary to measure the areas under the nuclear resonance peaks. Region I contains peaks corresponding to the protons attached to doubly bonded carbon atoms, while region II corresponds to protons attached to carbon atoms forming only single bonds. The ratio of areas (I:II) should be 3:1 for compound A and 1:1 for compound B. The measured value of 2.9:1 leaves no doubt of the identity of the sample with structure A.

The sample was furnished through the courtesy of  
Professor E. J. Corey, Chemistry Department, University of Illinois.

INCREASING MAGNETIC FIELD →



# 1961: FIRST WIDELY (WILDLY) SUCCESSFUL NMR INSTRUMENT

-Varian A-60 (60 MHz) NMR spectrometer

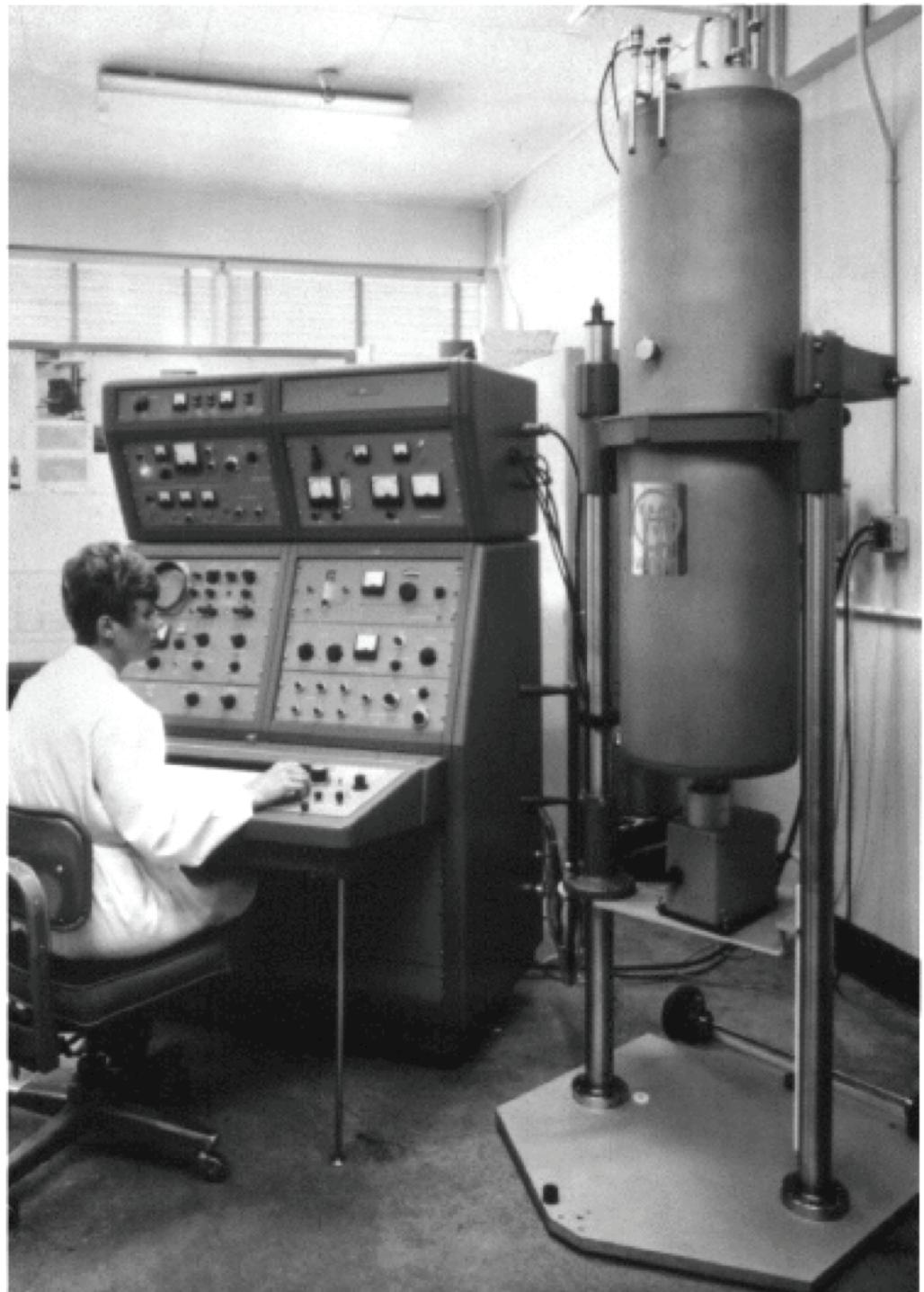


"I put a sample in the instrument, adjusted the resolution, and ran a spectrum on the precalibrated chart. It was perfect. But could the A-60 reproduce a spectrum with the fingerprint quality of the IR instrument? I moved the pen back to the start and restarted the scan. I was momentarily distracted, and when I looked back I saw only one line on the chart. "Why didn't the second scan run properly?" I asked. The answer came back, "It did!" Amazed and almost incredulous, I returned the pen three more times. It laid down five identical spectra with a single trace showing on the paper! ***At that instant, I knew the field of organic chemistry would never be the same again.***" (from Shoolery, J.N. "NMR spectroscopy in the beginning." *Anal. Chem.* **1993**, *65*(17), 731A-741A)

# SUPERCONDUCTING MAGNETS

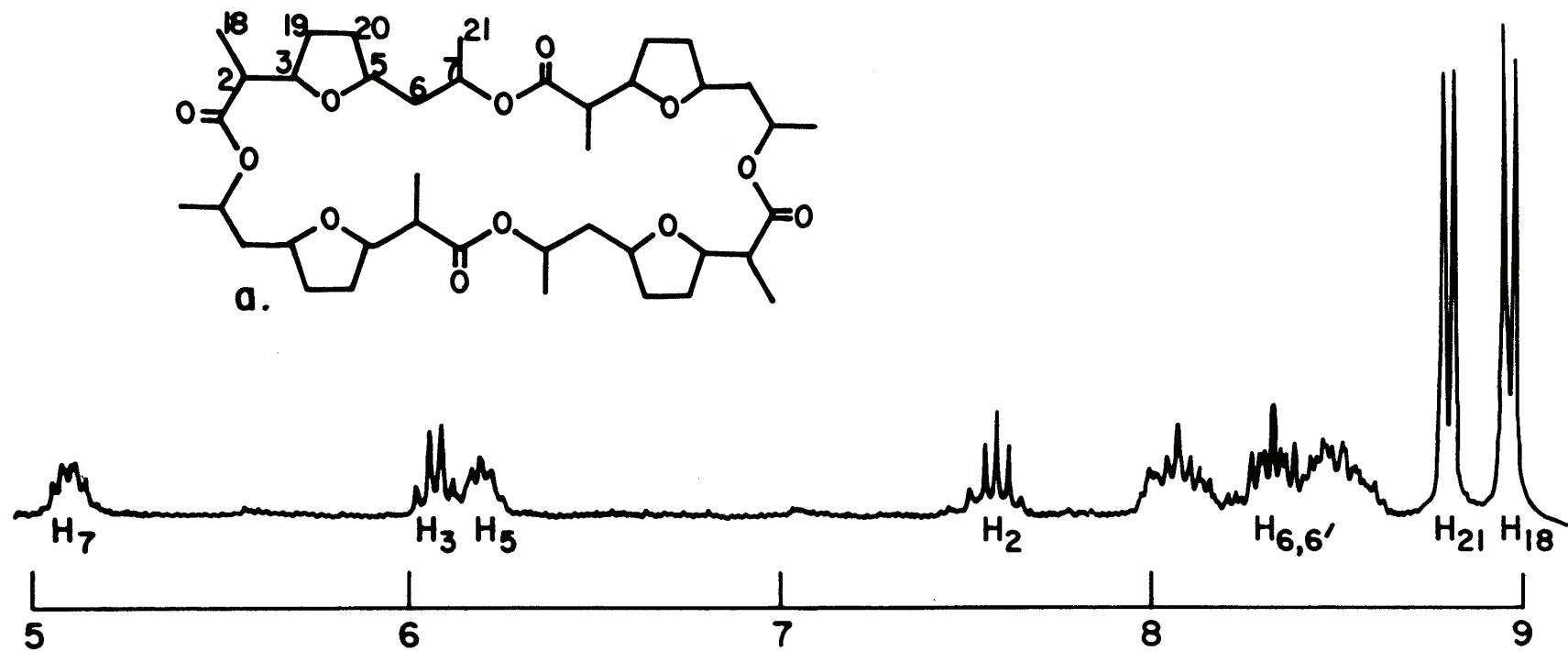
-the first high resolution superconducting NMR magnet (1964): the Varian HR-200, the HR-220 (shown here) and later the HR-300 high resolution NMR spectrometers.

-niobium-titanium alloy wire wrapped around a core and bathed in liquid helium (4 K)



# HIGH FIELD NMR

-high field (200 MHz), but still 1D CW NMR



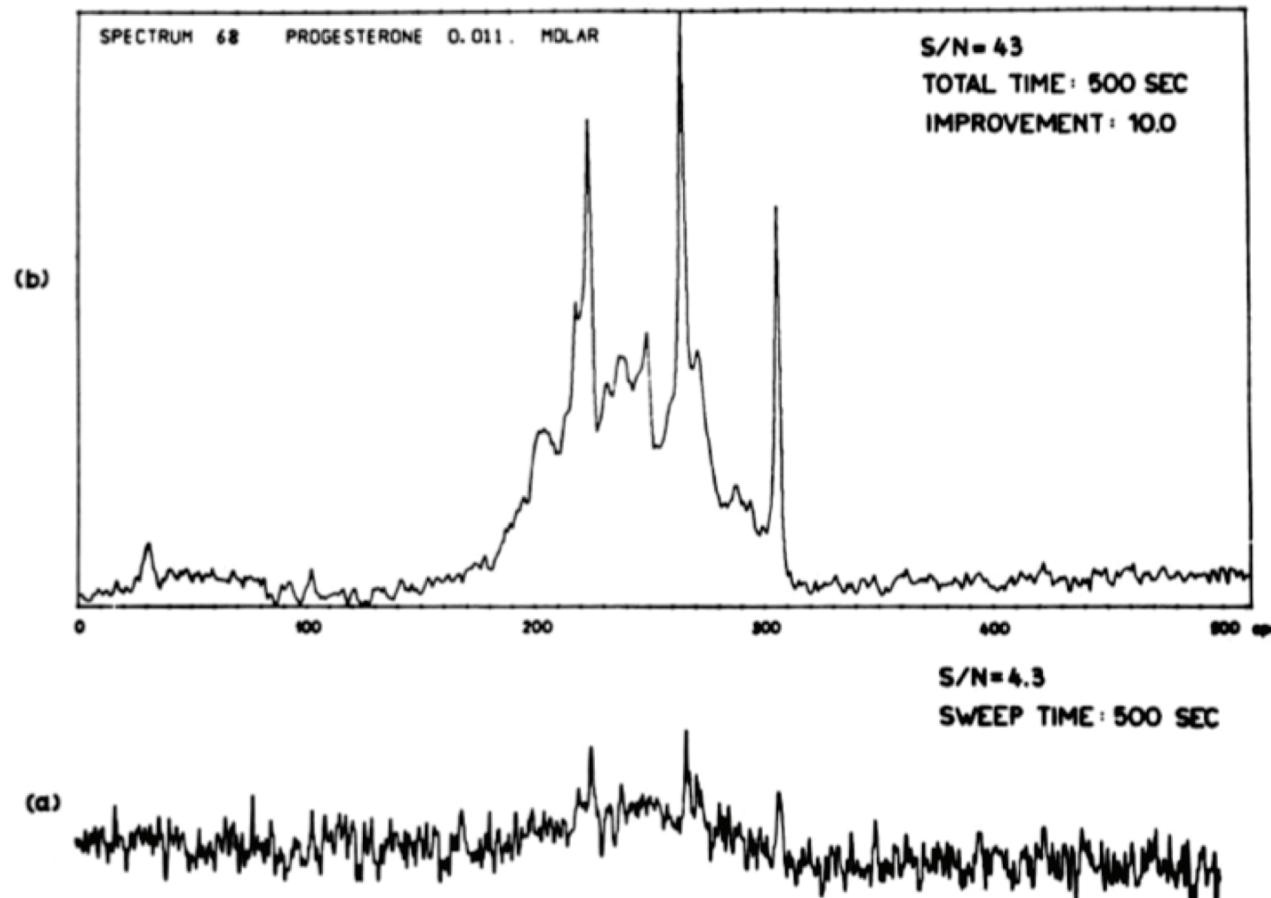
# 1966: PRIMATIVE COMPUTER CONTROL AND PULSED FOURIER TRANSFORM NMR

-Richard Ernst in 1965/1966 at the helm



# PULSED FOURIER TRANSFORM NMR

Richard Ernst & Wes Anderson, Rev. Sci. Instr. 37, 93 (1966)



Fourier transform (top) and conventional spectra of 0.011 M progesterone showing sensitivity enhancement by a factor ten

# MODERN SUPERCONDUCTING MAGNETS

