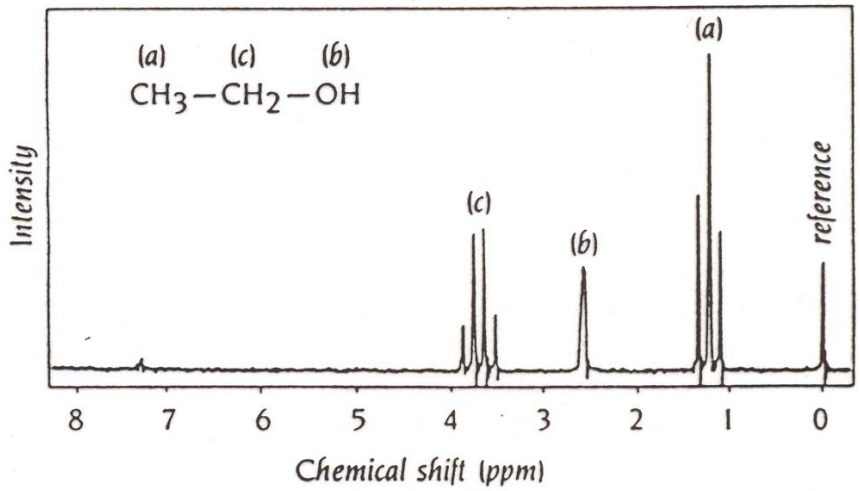
NMR Spectroscopy: Intro

NMR: Sophomore Organic Chemistry

- Sophomore organic NMR:
  - -1D, ^{1}H spectra
  - -small organic molecules
  - -one signal for each type of ^{1}H
  - -signals split into doublets, triplet, quartets, etc., due to presence of ^{1}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
H																H	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	*	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
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/NMRpertbl.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"

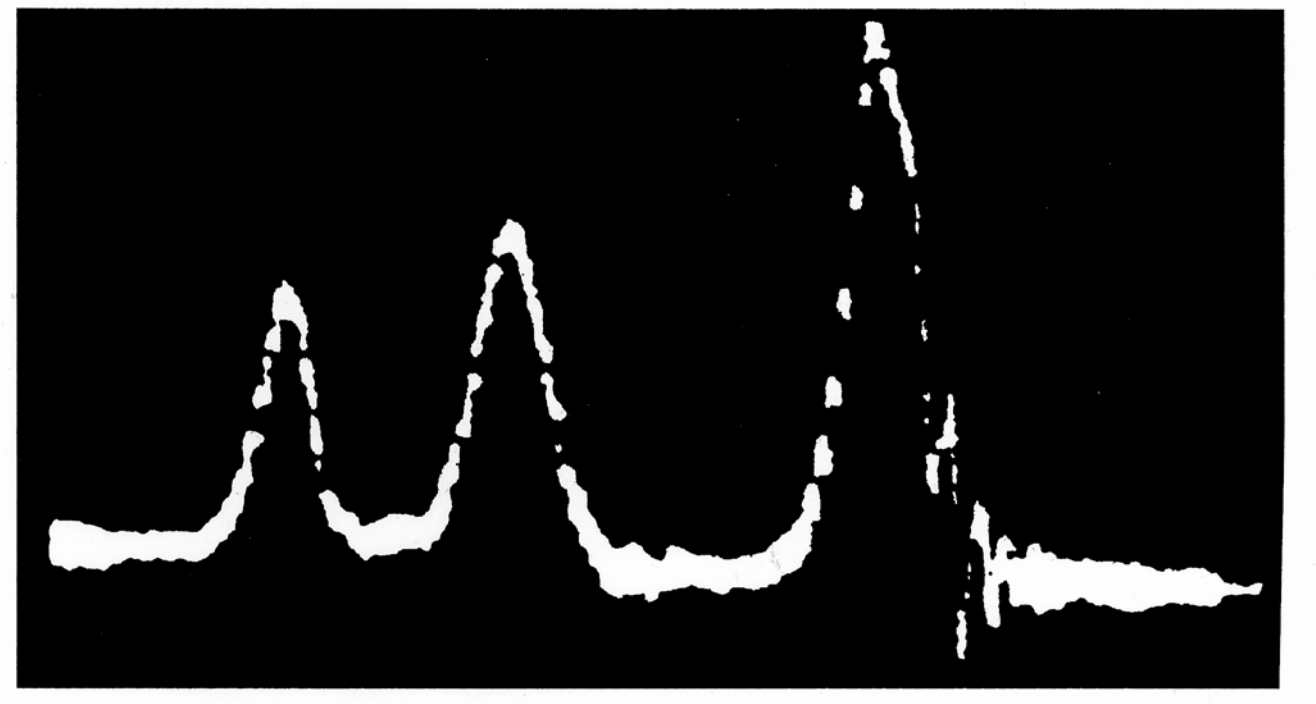
- 2003 – Paul Lauterbur and Sir Peter Mansfield – Nobel Prize in Physiology and Medicine

  -"for their discoveries concerning magnetic resonance imaging"

History

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

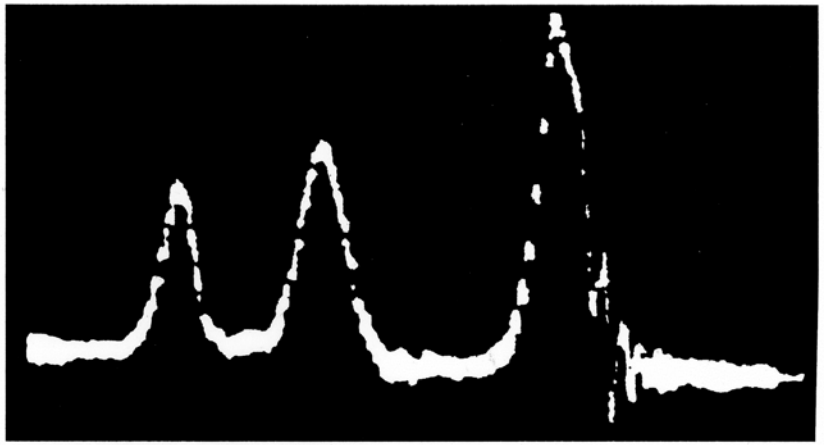
-spectrum of ethanol demonstrated that NMR spectra were a source of structural information (now, chemists got interested)



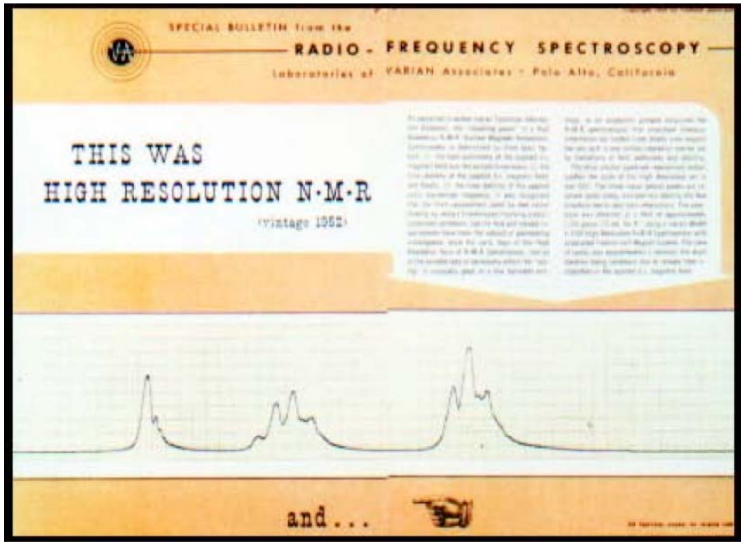
*Arnold, J. T., Dharmatti, S. S., and Packard, M. E., (1951) **Chemical Effects on Nuclear Induction Signals from Organic Compounds**. *J. Chem. Phys.* **19**, 507.

History

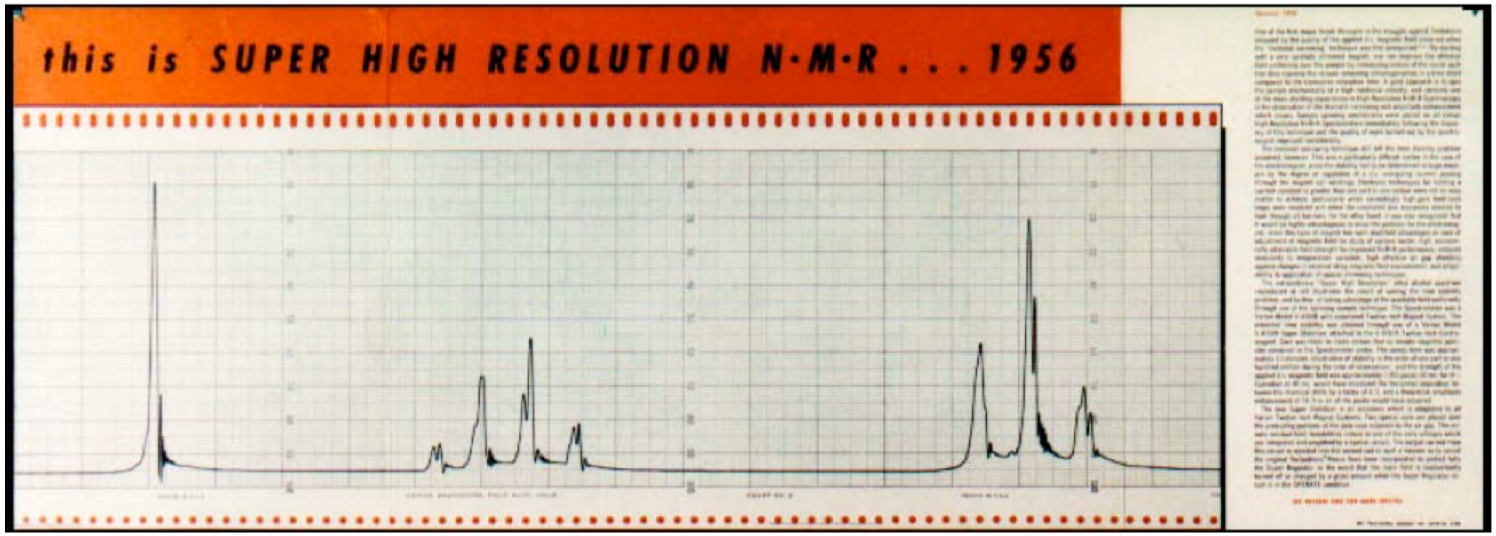
Ethanol - 1951



Ethanol - 1952

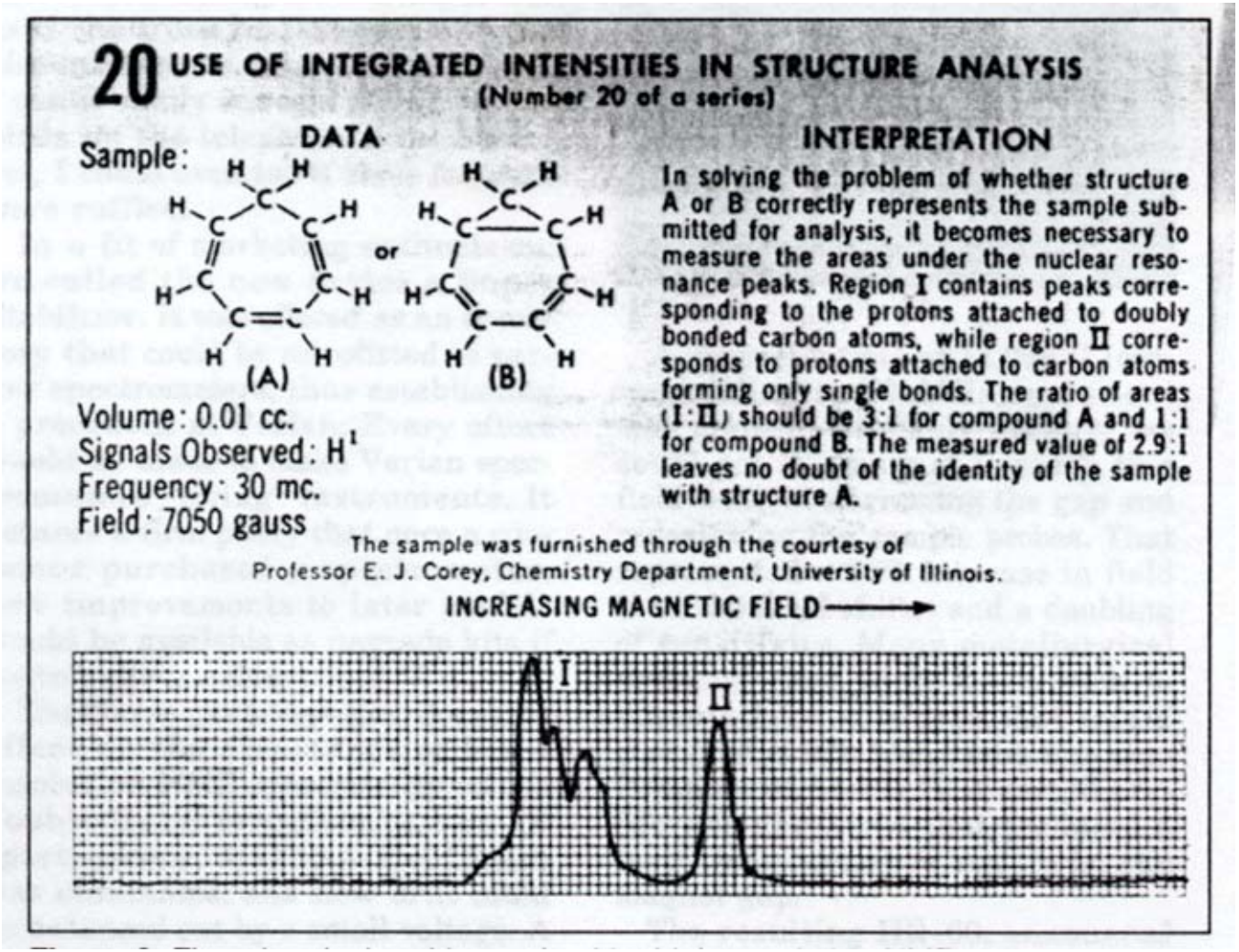


Ethanol - 1956



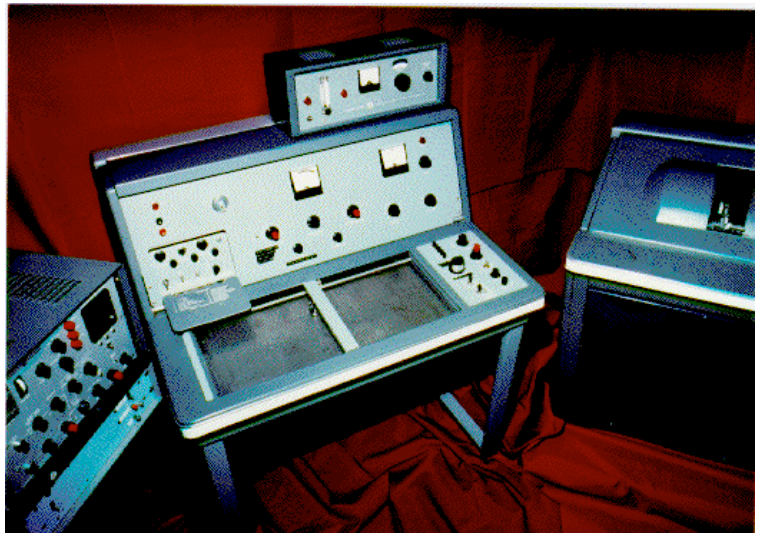
History

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



1961: First Widely (Wildly) Successful NMR Instrument

-Varian A-60 (60 MHz) NMR spectrometer

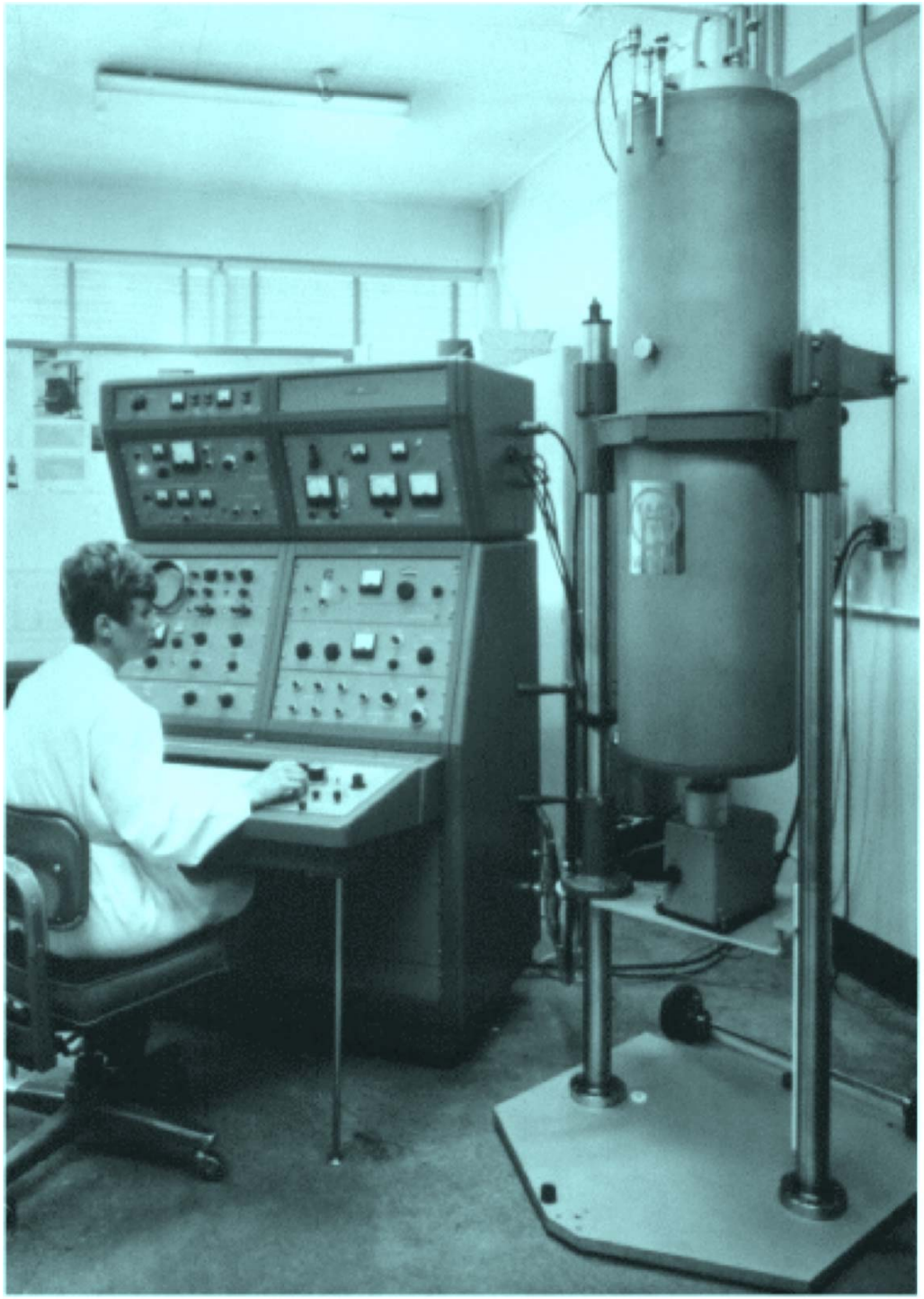


"I put a sample in the instrument, adjusted the resolution, and ran a spectrum on the precalibrated chart. It was perfect. But could the A-60 reproduce a spectrum with the fingerprint quality of the IR instrument? I moved the pen back to the start and restarted the scan. I was momentarily distracted, 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

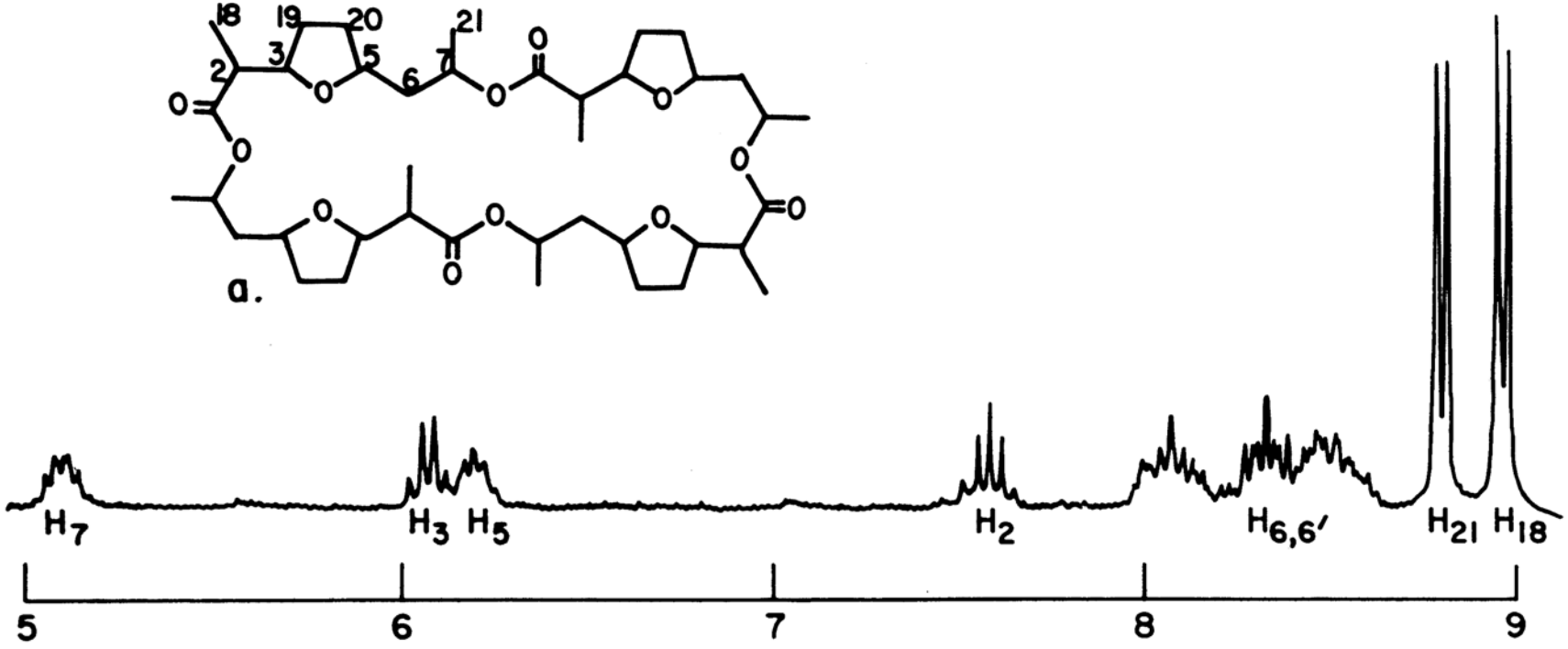
-the first high resolution superconducting NMR magnet (1964): the Varian HR-200, the HR-220 (shown here) and later the HR-300 high resolution NMR spectrometers.

-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

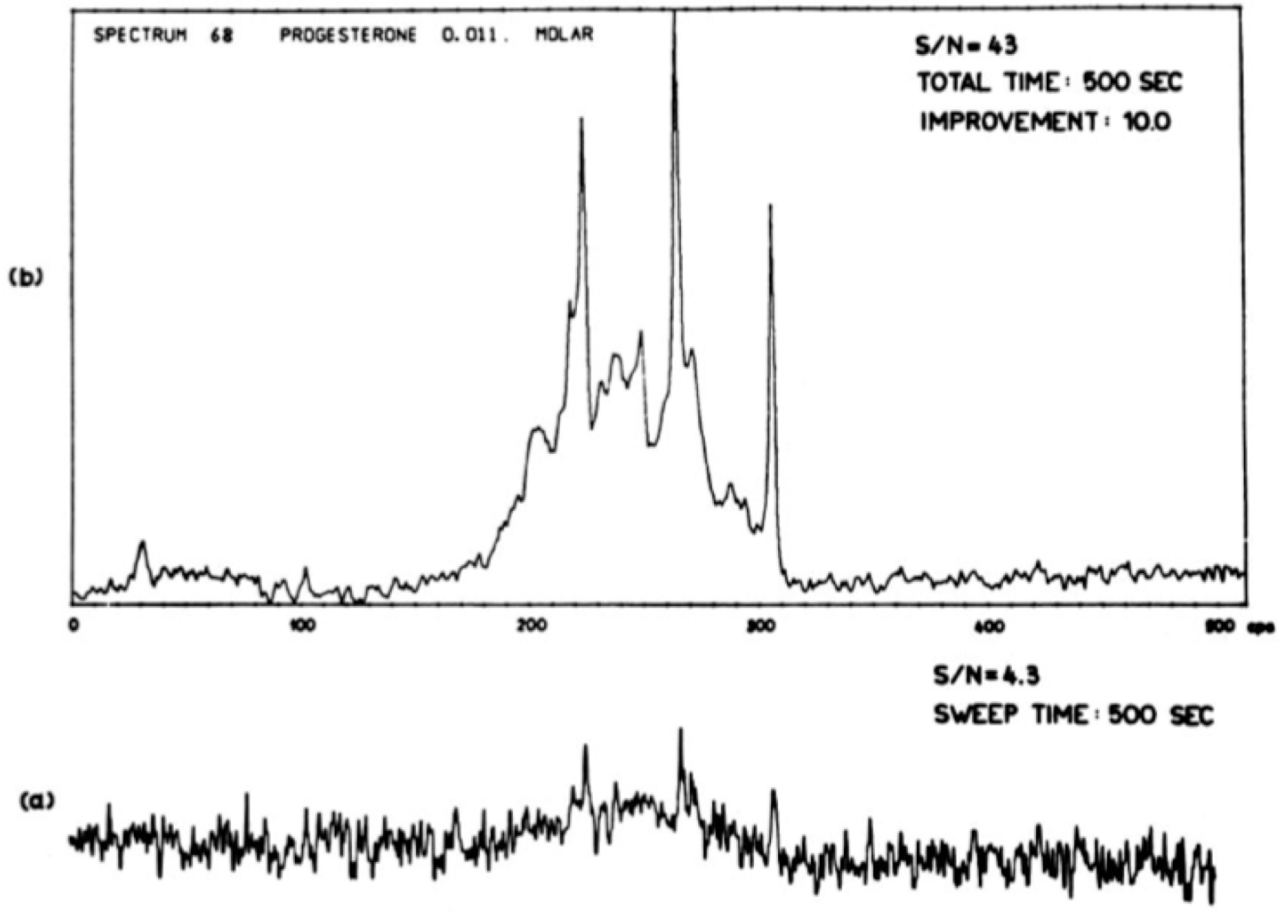


1966: Primative Computer Control And Pulsed Fourier Transform NMR

-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