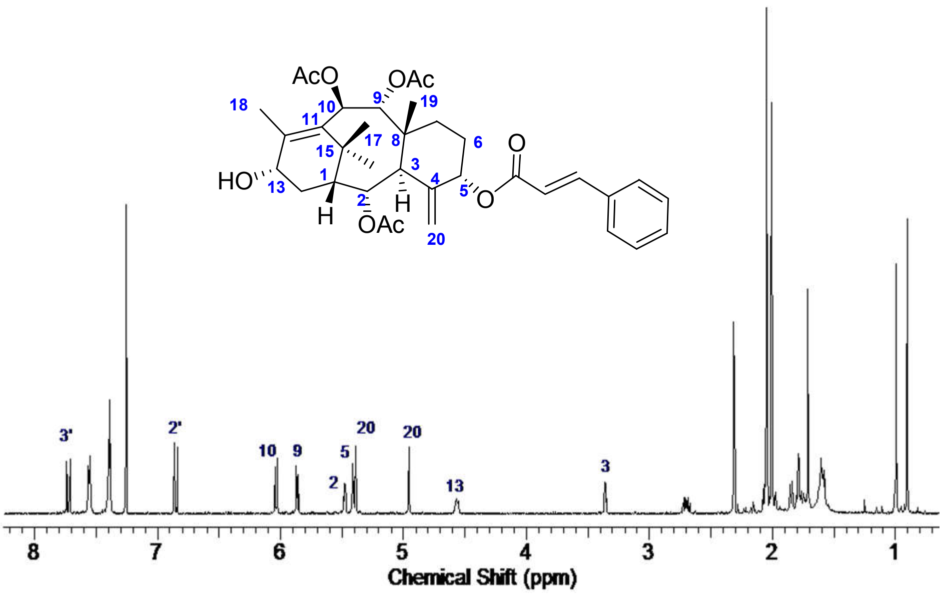
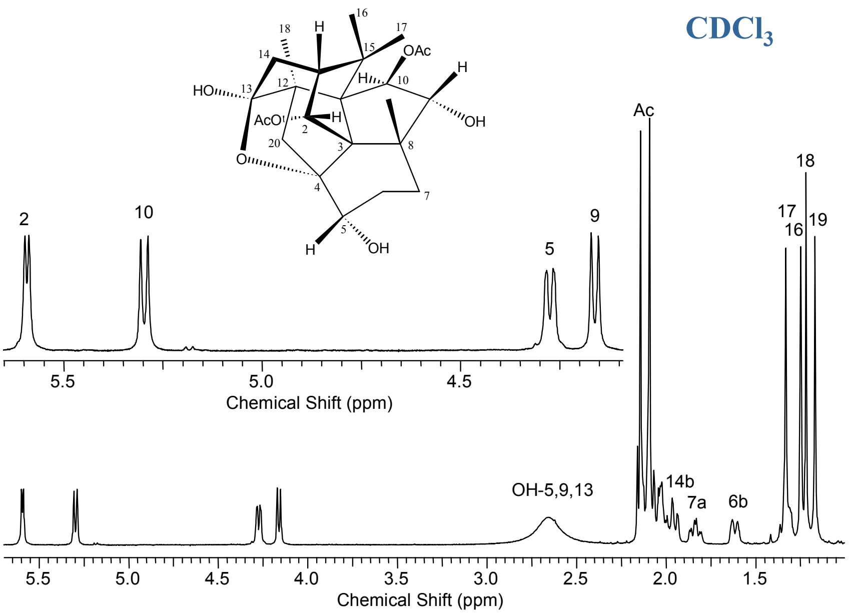
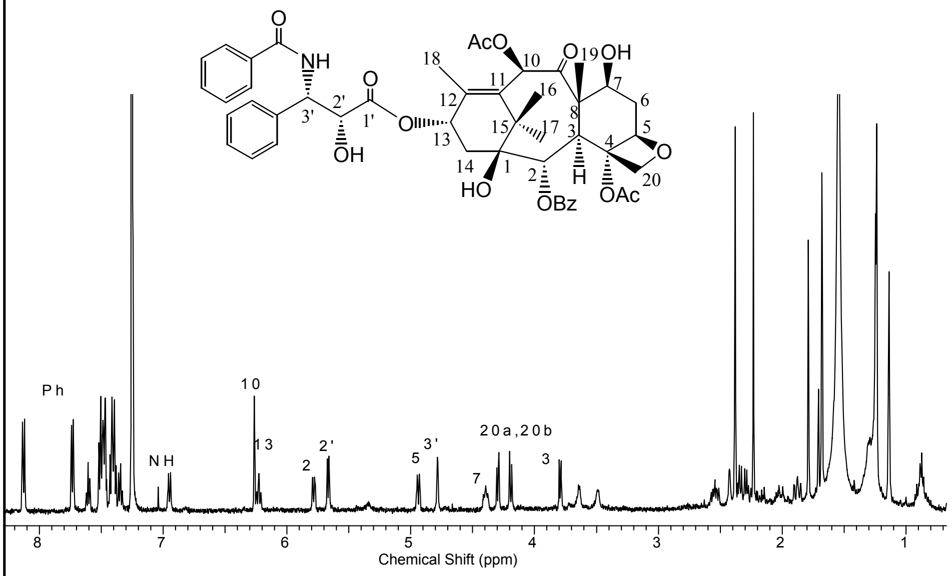
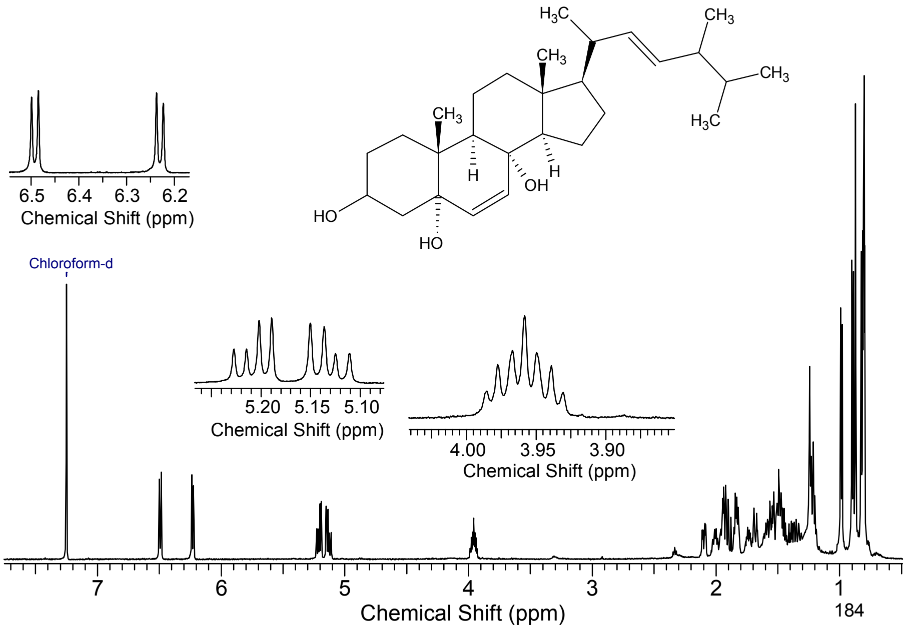

AcO
OAc
HO
OAc
H
H
O
O
18
11
10
9
19
15
17
8
6
13
1
3
4
5
2
20
3'
2'
10
9
2
5
20
20
13
3
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

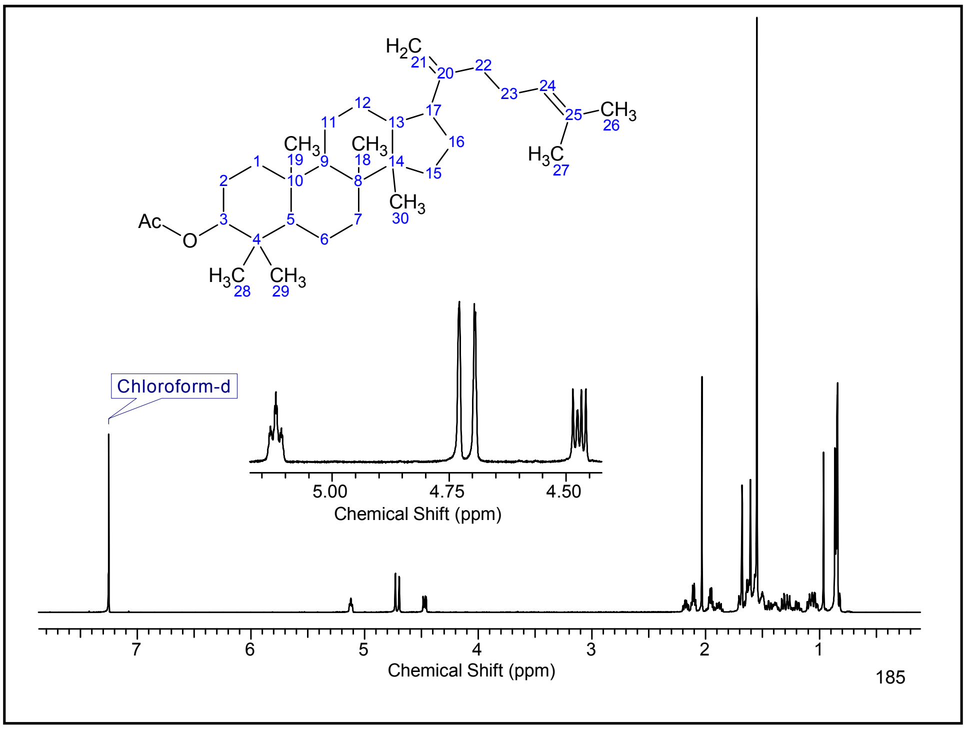
$CDCl_3$

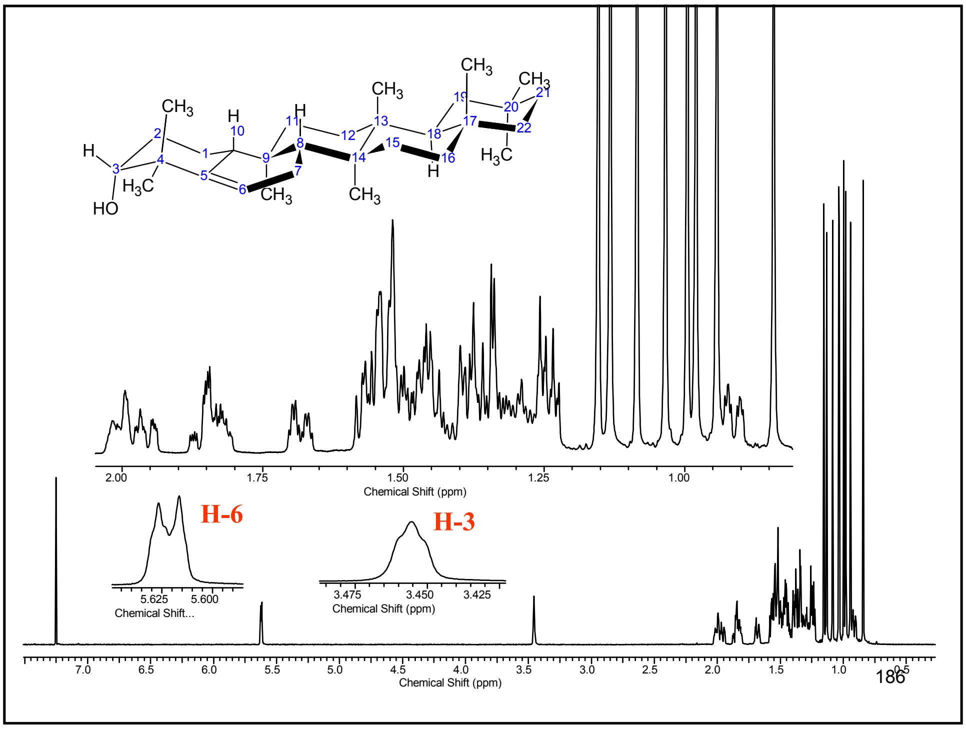

H
16
17
18
14
15
OAc
H
10
H
HO
13
12
AcO
2
H
OH
20
3
8
O
4
7
5
H
OH
2
10
5
9
5.5
5.0
4.5
Chemical Shift (ppm)
Ac
18
17
16
19
OH-5,9,13
14b
7a
6b
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)

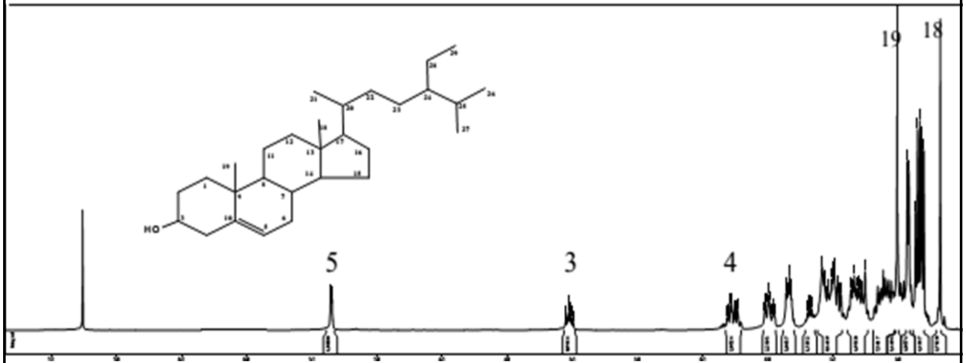
Taxol

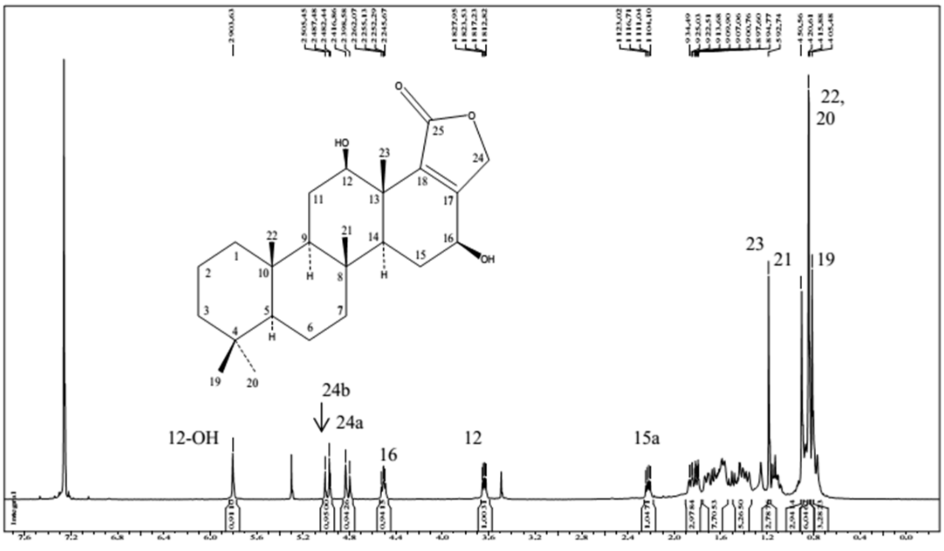

AcO
10
O
19
OH
7
6
5
O
18
11
12
16
15
17
8
3
4
13
14
1
2
H
HO
OBz
OAc
20
O
NH
O
3'
2'
1'
O
OH
Ph
10
13
NH
2'
2
5
3'
20a,20b
7
3
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

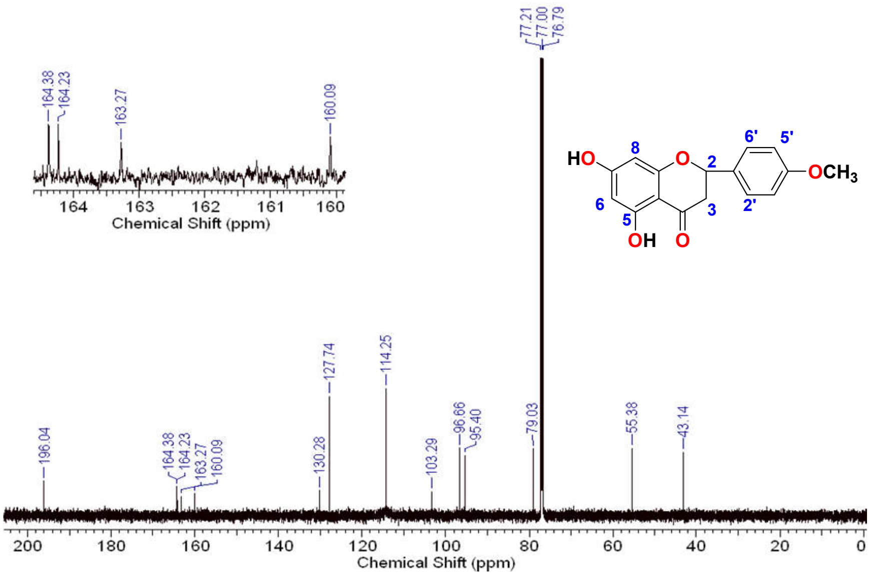

H$_3$C
CH$_3$
CH$_3$
CH$_3$
H$_3$C
CH$_3$
H
H
OH
HO
HO
6.5
6.4
6.3
6.2
Chemical Shift (ppm)
Chloroform-d
5.20
5.15
5.10
Chemical Shift (ppm)
4.00
3.95
3.90
Chemical Shift (ppm)
7
6
5
4
3
2
1
Chemical Shift (ppm)


H$_2$C
21
20
22
23
24
25
CH$_3$
26
H$_3$C
27
17
13
12
11
16
15
14
CH$_3$
19
CH$_3$
18
9
10
8
1
2
3
4
5
6
7
CH$_3$
30
Ac
O
H$_3$C
28
CH$_3$
29
Chloroform-d
5.00
4.75
4.50
Chemical Shift (ppm)
7
6
5
4
3
2
1
Chemical Shift (ppm)
185

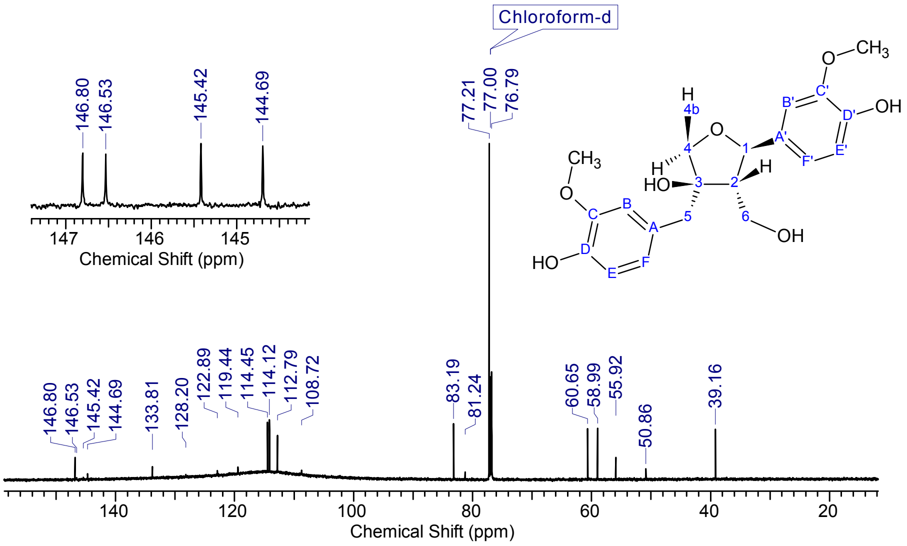

CH$_3$
CH$_3$
21
19
20
17
22
18
16
H$_3$C
H
13
CH$_3$
12
15
14
CH$_3$
H
11
8
7
9
CH$_3$
H
10
CH$_3$
2
1
5
6
H
3
4
H$_3$C
HO
2.00
1.75
1.50
1.25
1.00
Chemical Shift (ppm)
H-6
5.625
5.600
Chemical Shift...
H-3
3.475
3.450
3.425
Chemical Shift (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)
186


19
18
5
3
4
HO

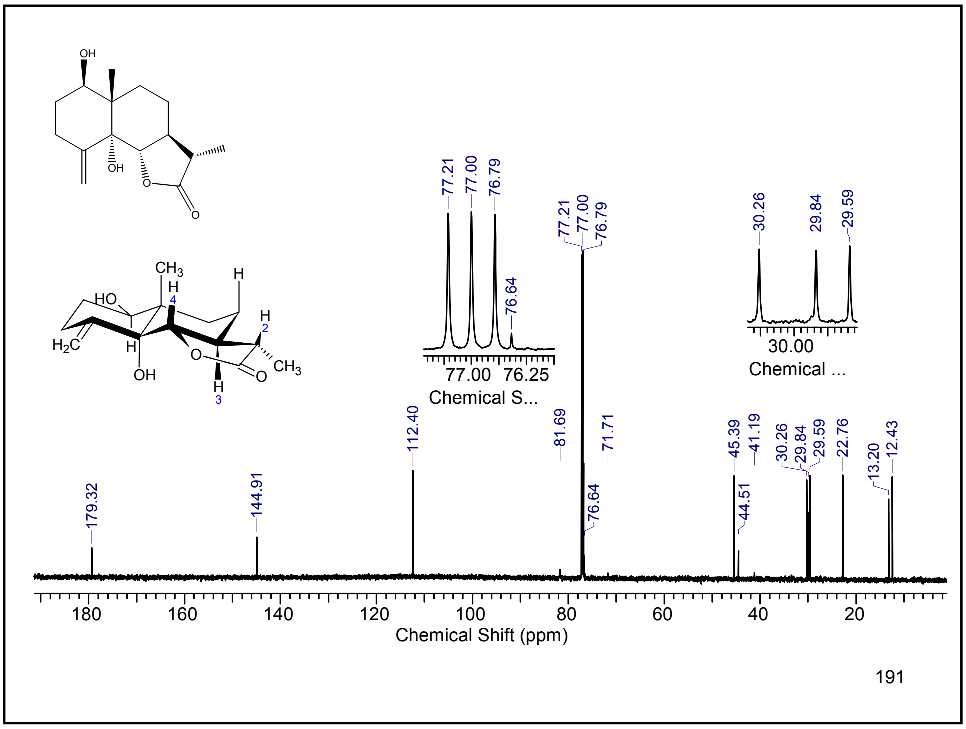

22,
20
23
21
19
12-OH
24b
24a
16
12
15a
OH
OH
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0

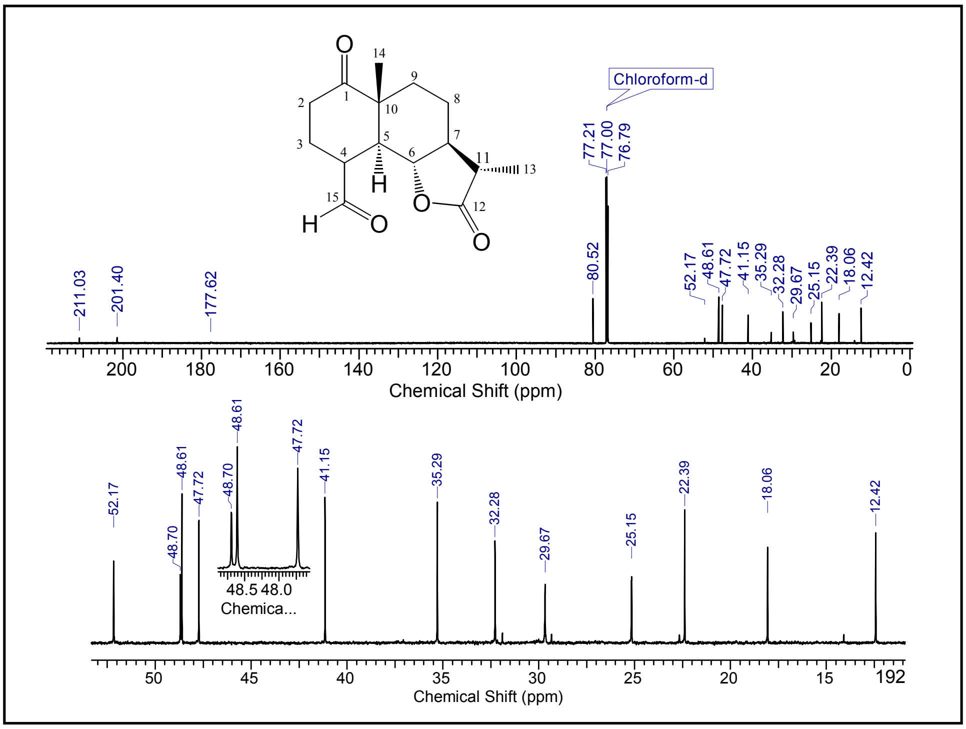

164.38
164.23
163.27
160.09
164
163
162
161
160
Chemical Shift (ppm)
77.21
77.00
76.79
HO
8
O
2
6'
5'
OCH3
6
5
3
2'
OH
O
196.04
164.38
164.23
163.27
160.09
130.28
127.74
114.25
103.29
96.66
95.40
79.03
55.38
43.14
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

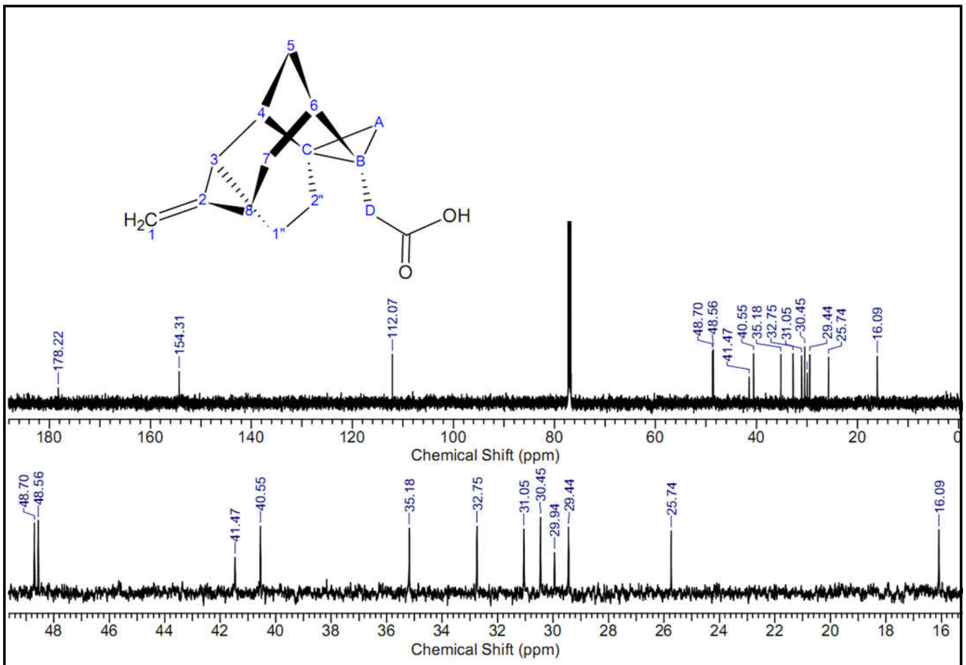
189

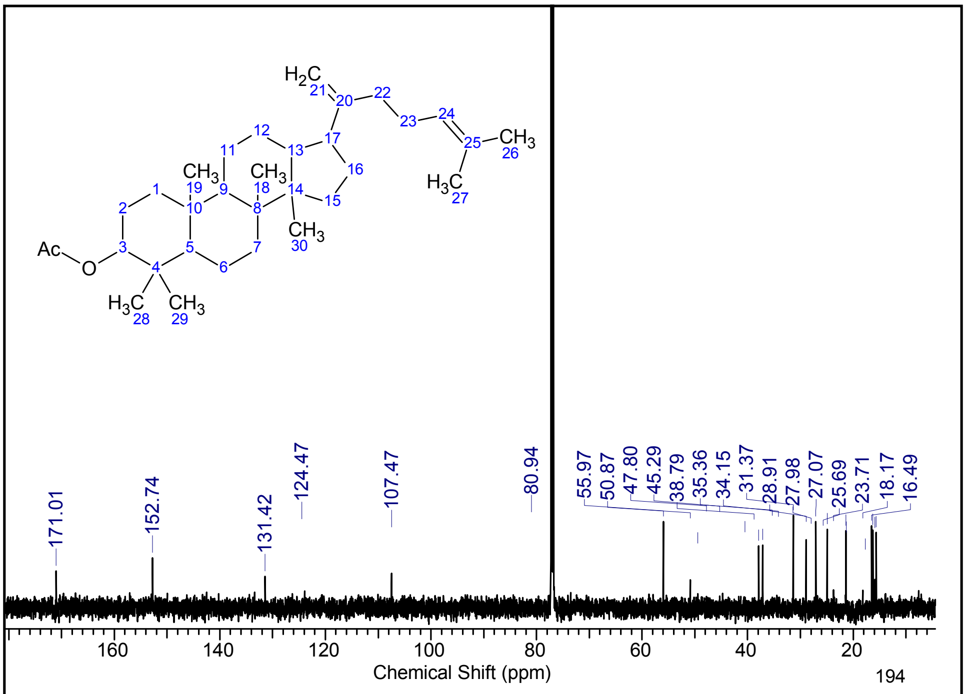

Chloroform-d
146.80
146.53
145.42
144.69
147
146
145
Chemical Shift (ppm)
77.21
77.00
76.79
CH3
O
B'
C'
D'
OH
A'
F'
E'
H
4b
O
4
1
H
HO
3
2
H
CH3
O
C
B
A
5
6
OH
HO
D
E
F
146.80
146.53
145.42
144.69
133.81
128.20
122.89
119.44
114.45
114.12
112.79
108.72
83.19
81.24
60.65
58.99
55.92
50.86
39.16
140
120
100
80
60
40
20
Chemical Shift (ppm)

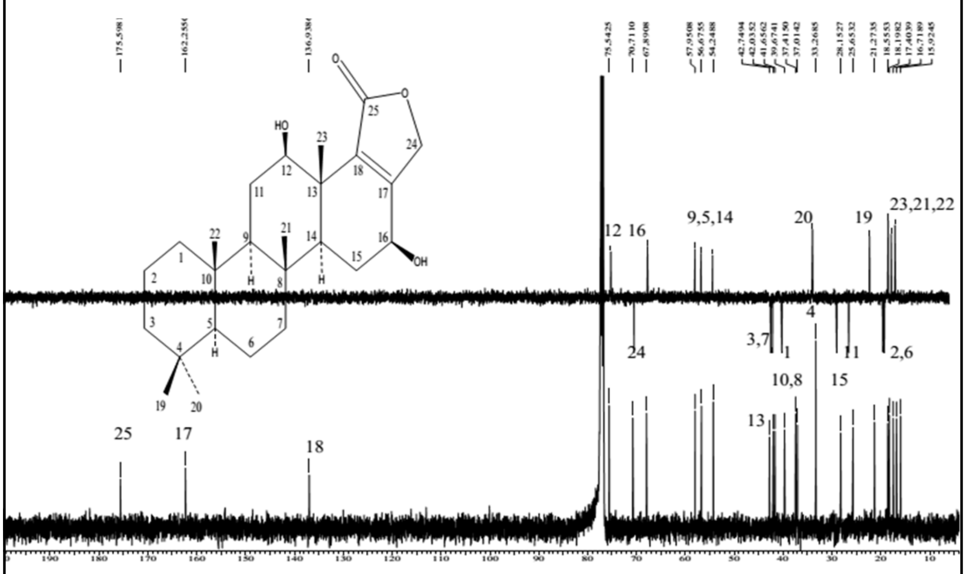
190

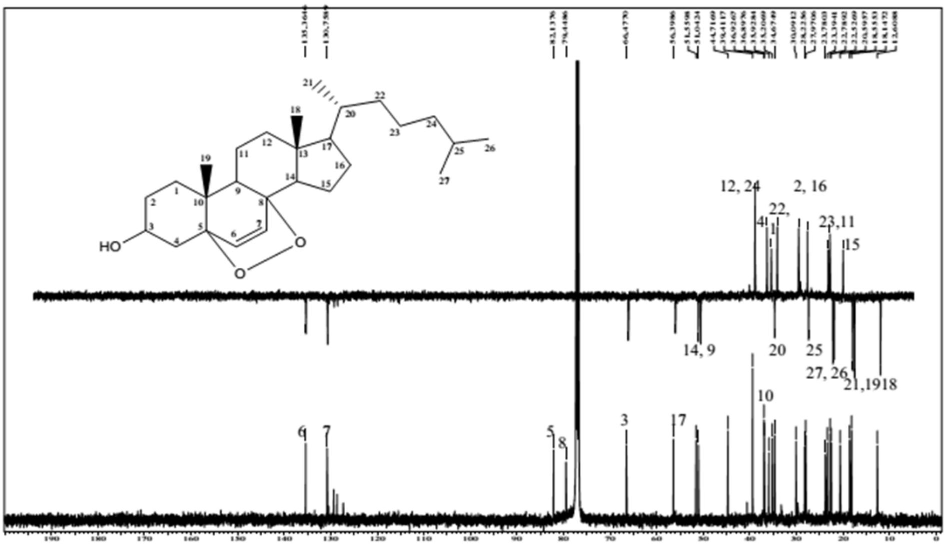

OH
OH
O
O
CH3
H
4
H
HO
2
H2C
H
O
CH3
OH
O
H
3
77.21
77.00
76.79
76.64
77.00 76.25
Chemical S...
77.21
77.00
76.79
30.26
29.84
29.59
30.00
Chemical ...
179.32
144.91
112.40
81.69
76.64
71.71
45.39
44.51
41.19
30.26
29.84
29.59
22.76
13.20
12.43
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)
191

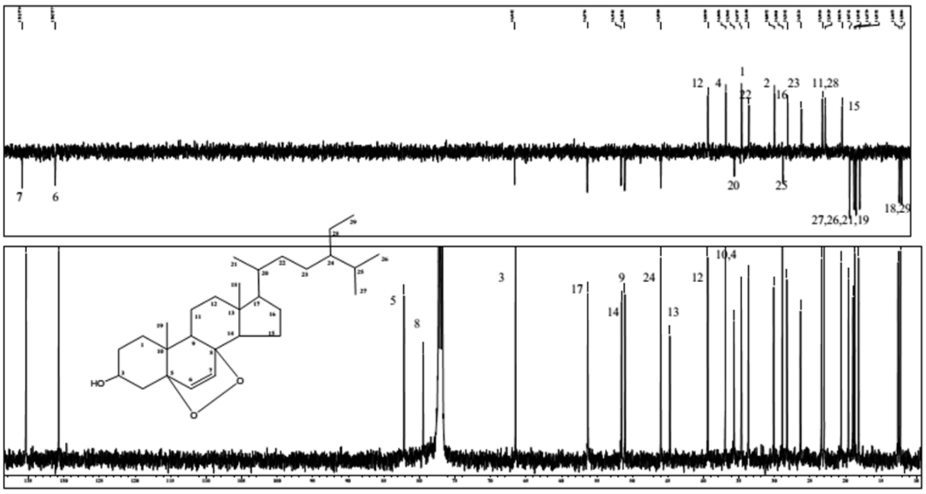

O
14
9
8
2
1
10
3
4
5
7
6
11
13
15
H
H
O
O
12
O
Chloroform-d
77.21
77.00
76.79
211.03
201.40
177.62
80.52
52.17
48.61
47.72
41.15
35.29
32.28
29.67
25.15
22.39
18.06
12.42
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
52.17
48.70
48.61
47.72
48.70
48.61
47.72
48.5 48.0
Chemica...
41.15
35.29
32.28
29.67
25.15
22.39
18.06
12.42
50
45
40
35
30
25
20
15
Chemical Shift (ppm)
192

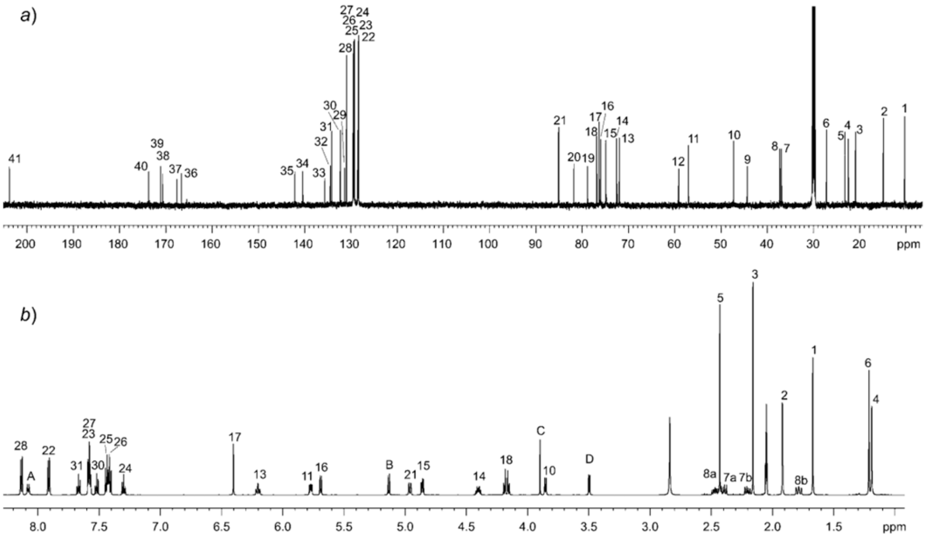

5
4
6
A
3
7
C
B
2
8
2"
D
OH
H_2C
1
1"
O
178.22
154.31
112.07
48.70
48.56
41.47
40.55
35.18
32.75
31.05
30.45
29.44
25.74
16.09
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
48.70
48.56
41.47
40.55
35.18
32.75
31.05
30.45
29.94
29.44
25.74
16.09
48
46
44
42
40
38
36
34
32
30
28
26
24
22
20
18
16
Chemical Shift (ppm)

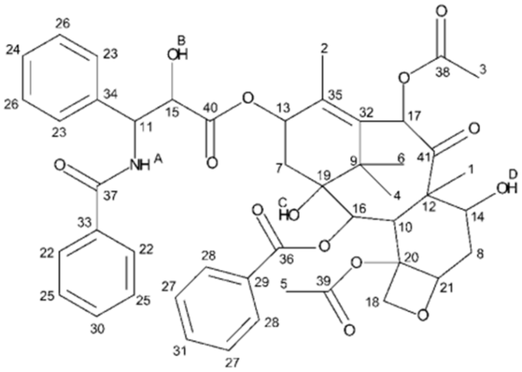

H_2C
21
20
22
23
24
25
CH_3
26
H_3C
27
12
17
11
13
16
CH_3
19
9
CH_3
18
14
15
1
2
10
8
Ac
O
3
5
7
6
CH_3
30
4
H_3C
28
CH_3
29
171.01
152.74
131.42
124.47
107.47
80.94
55.97
50.87
47.80
45.29
38.79
35.36
34.15
31.37
28.91
27.98
27.07
25.69
23.71
18.17
16.49
160
140
120
100
80
60
40
20
Chemical Shift (ppm)


175.5981
162.2550
136.9380
75.5425
70.7110
67.8908
57.9508
56.6755
54.2488
42.7494
42.0352
41.6562
39.6741
37.4150
37.0142
33.2685
28.1527
25.6532
21.2735
18.5553
18.1982
17.4039
16.7189
15.9245
O
O
25
24
HO
23
12
18
11
13
17
22
9
21
14
16
15
OH
1
2
10
8
3
5
7
4
6
H
H
H
19
20
12 16
9,5,14
20
19
23,21,22
24
3,7
1
4
11
2,6
10,8
15
13
25
17
18
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


135.3644
130.7589
82.1376
79.4486
66.4770
56.3986
51.5598
51.0424
44.7169
39.4117
36.9267
36.8976
35.9284
35.2069
34.6749
30.0912
28.2236
27.9706
23.7803
23.3941
22.7892
22.5269
20.5957
18.5553
18.1472
12.6088
21
22
18
20
23
24
25
26
27
19
12
17
11
13
16
1
9
14
15
2
10
8
3
5
6
7
HO
4
O
O
12, 24
2, 16
4
22,
1
23,11
15
14, 9
20
25
27, 26
21,1918
10
6
7
5
8
3
17
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


12
4
1
22
2
16
23
11,28
15
7
6
20
25
27,26,21,19
18,29
5
8
3
17
9
14
24
13
12
10,4
HO
O
O


a)
41
40
39
38
37
36
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
b)
28
A
22
31
27
23
30
25
26
24
17
13
11
16
B
21
15
14
18
C
10
D
8a
7a
7b
8b
3
5
2
1
6
4
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm



Taxol (**1**)

推导结构

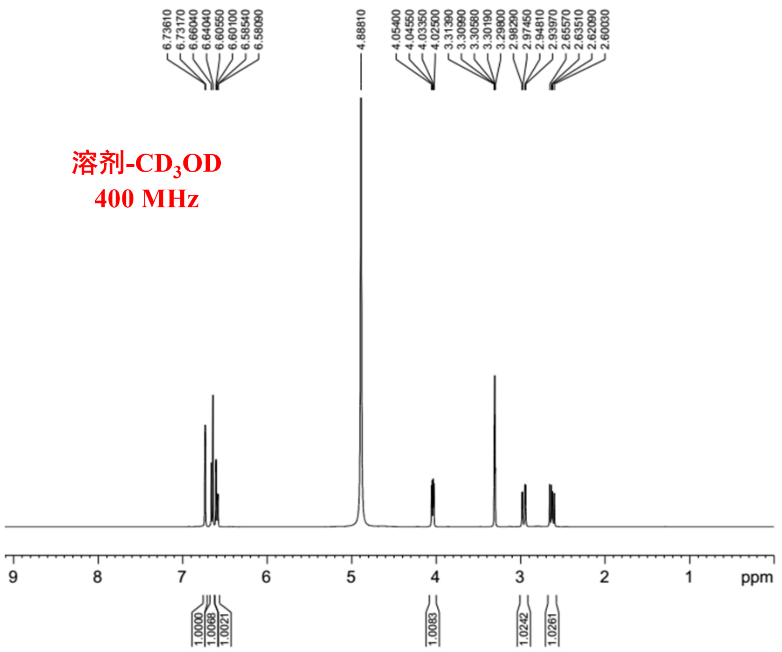
从某一常见中药的根中分离得到一个化合物，HR-MS 给出分子式是 $C_9H_{10}O_5$。

^{1}H-NMR 和^{13}C-NMR图谱如下。

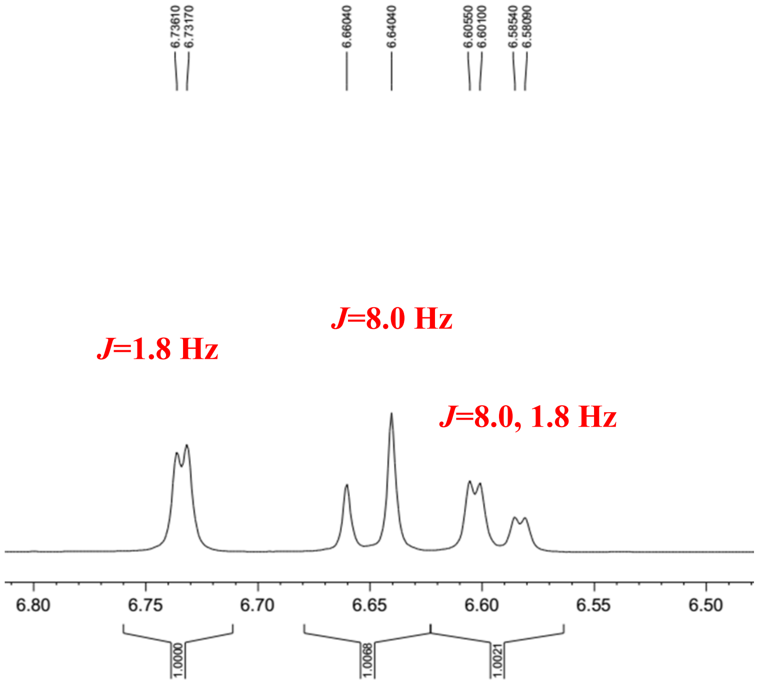
试推导其可能的结构。

Danshensu $C_9H_{10}O_5$

溶剂-CD_3OD
400 MHz



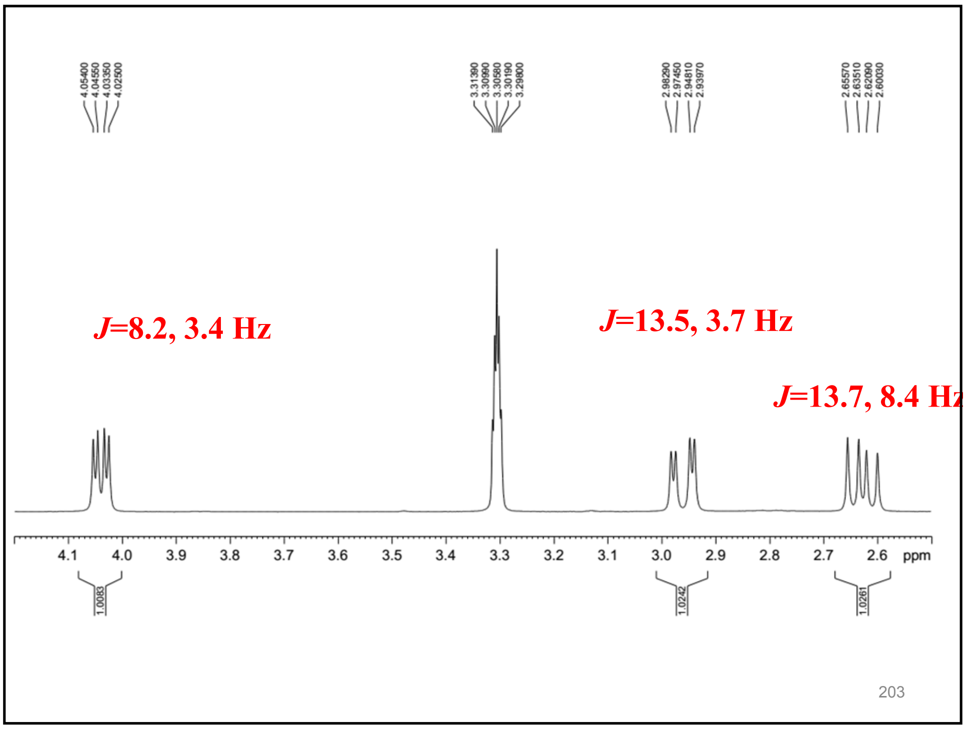
```
F2 - Acquisition Parameters
Date_          20050408
Time             13.39
INSTRUM          av400
PROBHD   5 mm DUL 13C-1
PULPROG           zg30
TD               65536
SOLVENT           MeOD
NS                  32
DS                   0
SWH       9980.040 Hz
FIDRES    0.152283 Hz
AQ       3.2834036 sec
RG                  64
DW         50.100 usec
DE           6.00 usec
TE             294.8 K
D1     1.00000000 sec
MCREST    0.00000000 se
MCWRK     0.01500000 se

======== CHANNEL f1 ====
NUC1                1H
P1          12.50 usec
PL1           -2.00 dB
SFO1    400.1318925 MHz

F2 - Processing parameters
SI               32768
SF     400.1300091 MHz
WDW                 EM
SSB                  0
LB             0.30 Hz
GB                   0
PC                1.00
```



J=1.8 Hz

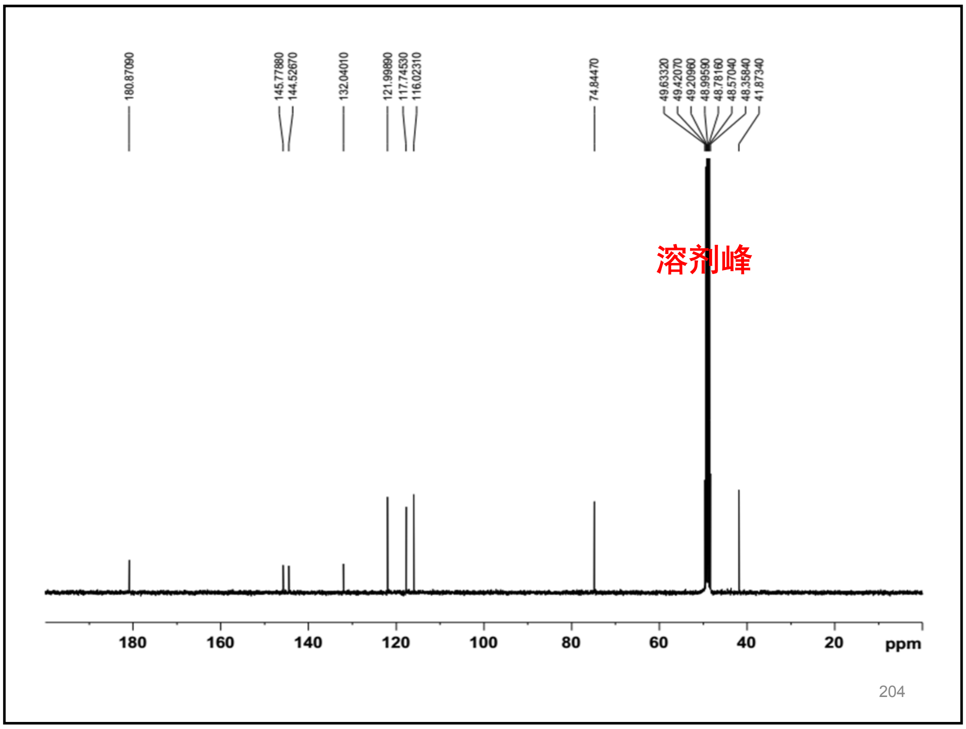
J=8.0 Hz

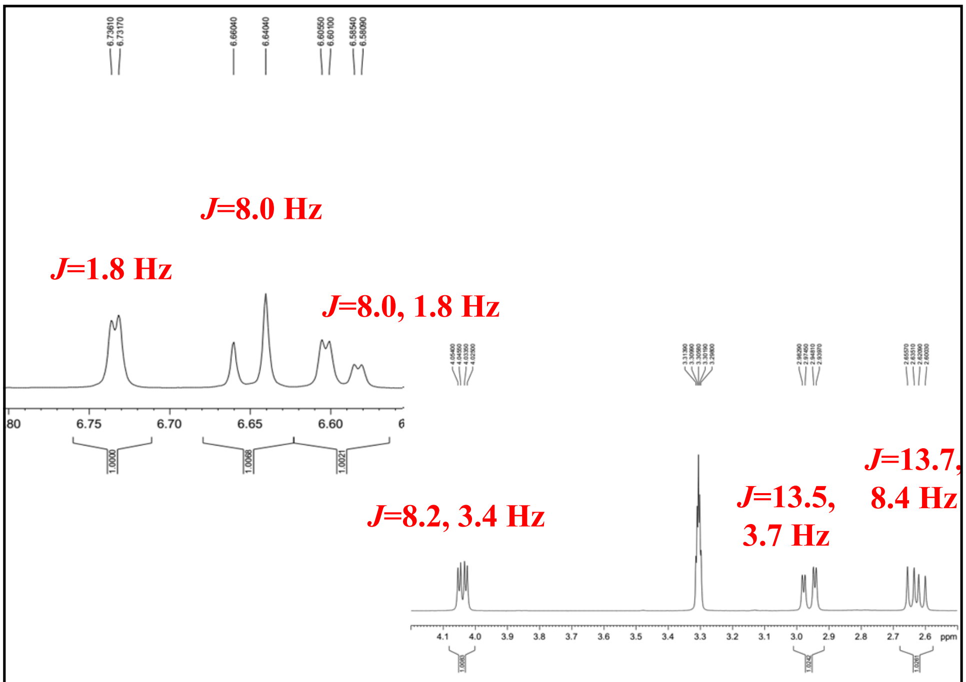
J=8.0, 1.8 Hz


J=8.2, 3.4 Hz

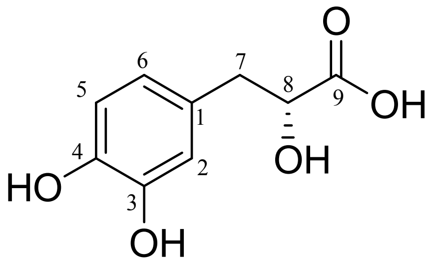
J=13.5, 3.7 Hz

J=13.7, 8.4 Hz


溶剂峰



丹参素

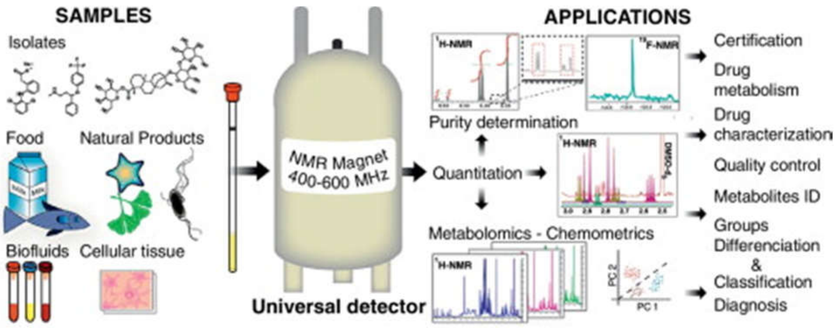


$C_9H_{10}O_5$

Exact Mass: 198.05

Nuclear Magnetic Resonance

^{1}H- and ^{13}C-NMR



Current Opinion in Biotechnology **2014**, *25*: 51-59.

Strategy of Structure Elucidation

UV
IR
HR-MS
→
共轭体系, 顺反构型
官能团 **C=O, C=C**
分子式: 双键, 环数, 杂原子

1D NMR
^{1}H-NMR
^{13}C-NMR
NOE
DEPT
→
H的个数和相互关系
C的个数和SP, SP^{2}, SP^{3}
H的空间关系
C的种类C, CH, CH$_{2}$, CH$_{3}$

2D NMR
^{1}H-^{1}H COSY H-C-C-H, H-C-H
HMQC H-C
HMBC H-C-C, H-C-C-C, H-C-C=C-C
NOESY (ROESY) H-H conformation
INADEQUATE C-C

X-Crystallography: Crystalline sample

核磁共振波谱法

核磁共振（Nuclear Magnetic Resonance，NMR）：

在外加磁场作用下，某些原子核能产生核自选能级分裂，当用一定频率的射频照射分子时。可引起原子核自旋能级的跃迁，吸收一定频率的射频，即产生核磁共振。

核磁共振波谱（NMR spectrum）：

以核磁共振信号强度对照射频率（或磁场强度）作图，即为核磁共振波谱。

核磁共振波谱法（NMR spectroscopy）：

利用核磁共振波谱进行结构（构型和构象）测定、定性及定量分析的方法。

Nuclear Magnetic Resonance

核磁场共振(NMR)被誉为有机物的指纹，它使有机物的鉴定和结构测定进入了一个新的阶段。

核磁共振谱(Nuclear Magnetic Resonance Spectroscopy—NMR)是指：低能电磁波（波长约106---109μm)与暴露在磁场中的磁性核相互作用，使其在外磁场中发生能级的共振跃迁而产生吸收信号，称为核磁共振谱。

Three Waves of NMR

第一阶段

1945～46年：F. Bloch 和 E. M. Purcell
两个小组几乎同时发现NMR现象

1950年代初：NMR首次应用于有机化学

1960年代初：Varian Associates A60 Spectrometer
问世，NMR开始广泛应用

第二阶段

1970年代：Fourier Transform的应用
^{13}C-NMR技术（碳骨架）
(GC，TLC，HPLC技术的发展)

第三阶段

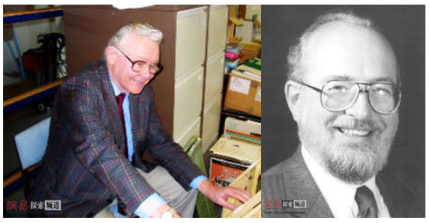
1980年代：Two-dimensional (2D) NMR诞生
(COSY，碳骨架连接顺序，非键原子间距离，生物大分子结构，……)

对NMR作过贡献的15位Nobel奖得主

1. 1944: I. Rabi
2. 1952: F. Bloch
3. 1952: E. M. Purcell
4. 1955: W. E. Lamb
5. 1955: P. Kusch
6. 1964: C. H. Townes
7. 1966: A. Kastler
8. 1977: J. H. Van Vleck
9. 1981: N. Bloembergen
10. 1983: H. Taube
11. 1989: N. F. Ramsey
12. 1991: R. R. Ernst

13 2002: Kurt Wiithrich

14. 2003: Paul Lauterbur and Peter Mansfield
15. 2013：Martin Karplus



Applications:

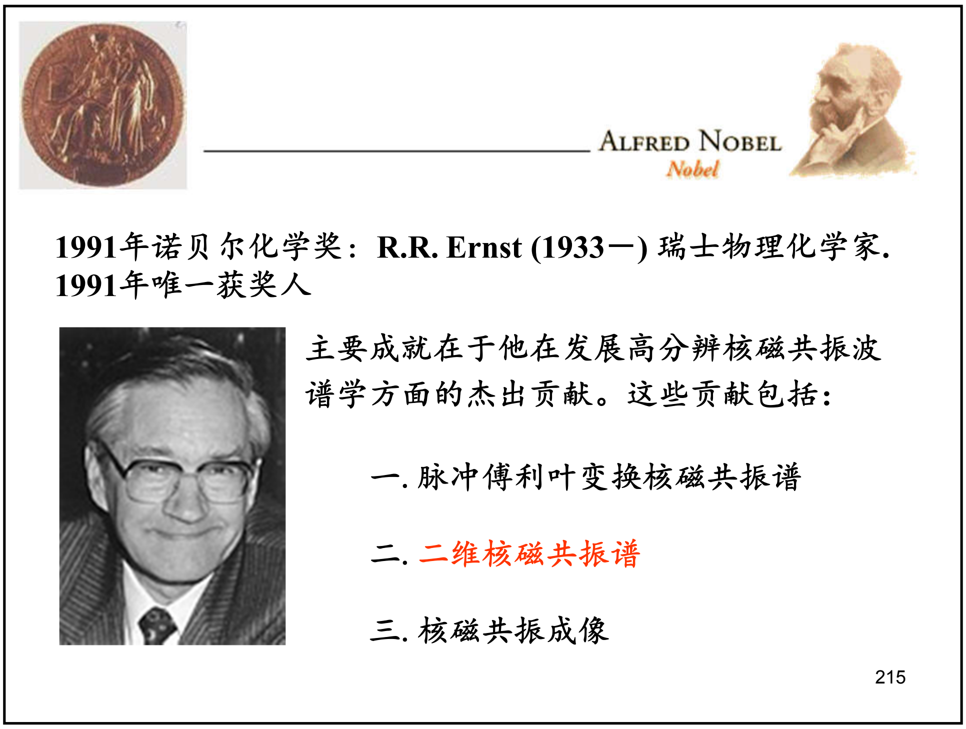
核磁共振已在众多领域中有了广泛的应用. 从技术手段上讲，核磁共振的应用主要有两个方面：

Ⅰ 核磁共振波谱：实际上是吸收率（纵坐标）对化学位移（横坐标）的关系曲线

Ⅱ 核磁共振成象（MRI）：（1） 点成像法

（2） 弛豫时间成像法

Nuclear Magnetic Resonance Imaging also called Spin Imaging



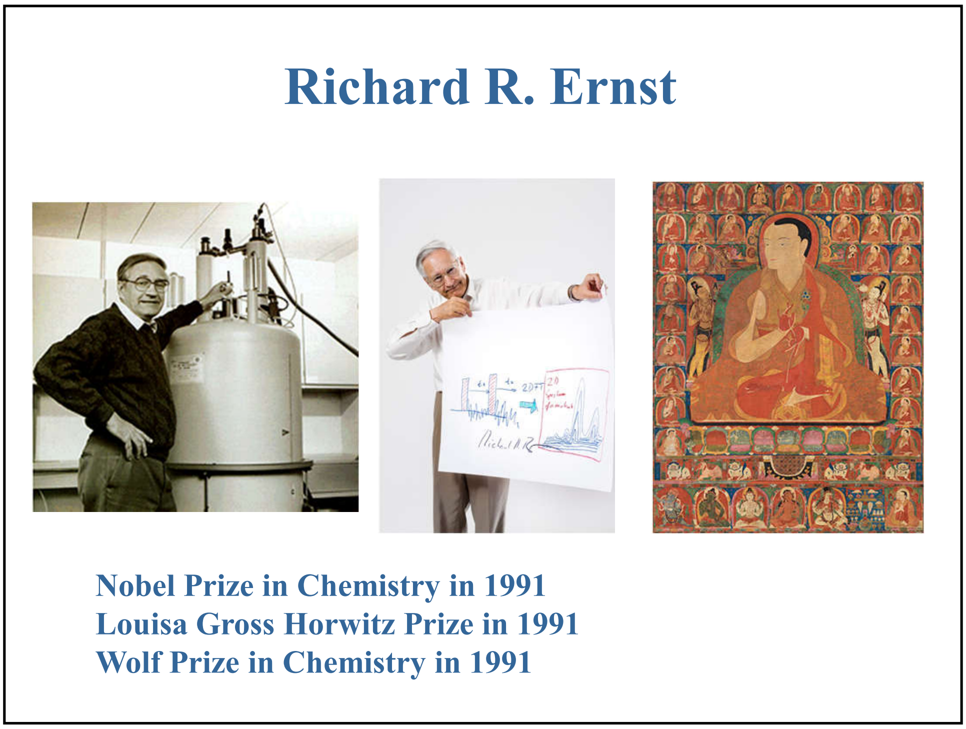
1991年诺贝尔化学奖：R.R. Ernst (1933—) 瑞士物理化学家.
1991年唯一获奖人

主要成就在于他在发展高分辨核磁共振波谱学方面的杰出贡献。这些贡献包括：

一. 脉冲傅利叶变换核磁共振谱

二. 二维核磁共振谱

三. 核磁共振成像

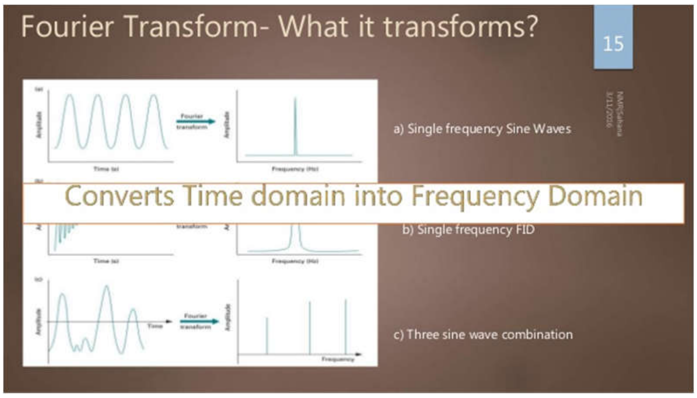


Richard R. Ernst

Nobel Prize in Chemistry in 1991
Louisa Gross Horwitz Prize in 1991
Wolf Prize in Chemistry in 1991

The Fourier Transform

Jean-Baptiste J. Fourier



Fourier Transform- What it transforms?

15

a) Single frequency Sine Waves

Converts Time domain into Frequency Domain

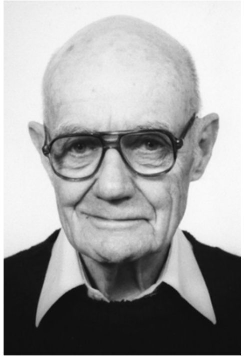
b) Single frequency FID

c) Three sine wave combination

NMRSahana 3/11/2016

Jean-Baptiste J. Fourier (1768-1830) was a French mathematician and physicist. He is best known for initiating the investigation of Fourier series and their applications to problems of heat transfer and vibrations. The Fourier transform and Fourier's law are also named in his honour. Fourier is also generall credited with the discovery of the greenhouse effect

The Nobel Prize in Chemistry 2002



John B. Fenn

Koichi Tanaka

Kurt Wüthrich

Kurt Wüthrich and NMR of Biological Macromolecules

Kurt Wüthrich

Richard R. Ernst

1985年,利用Kurt Wuthrich 的方法确定了第一个蛋白质的结构。

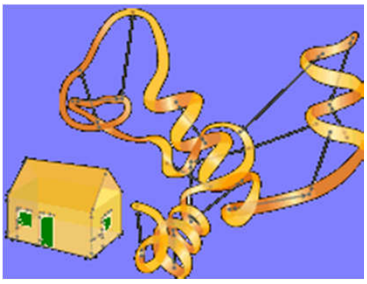
2017年12月， Kurt Wuthrich成为首批来沪工作并拥有“中国绿卡”的诺奖得主。

Wüthrich collaborated with, among others, Nobel laureate Richard R. Ernst on developing the first two-dimensional NMR experiments, and established the NOE as a convenient way of measuring distances within proteins.

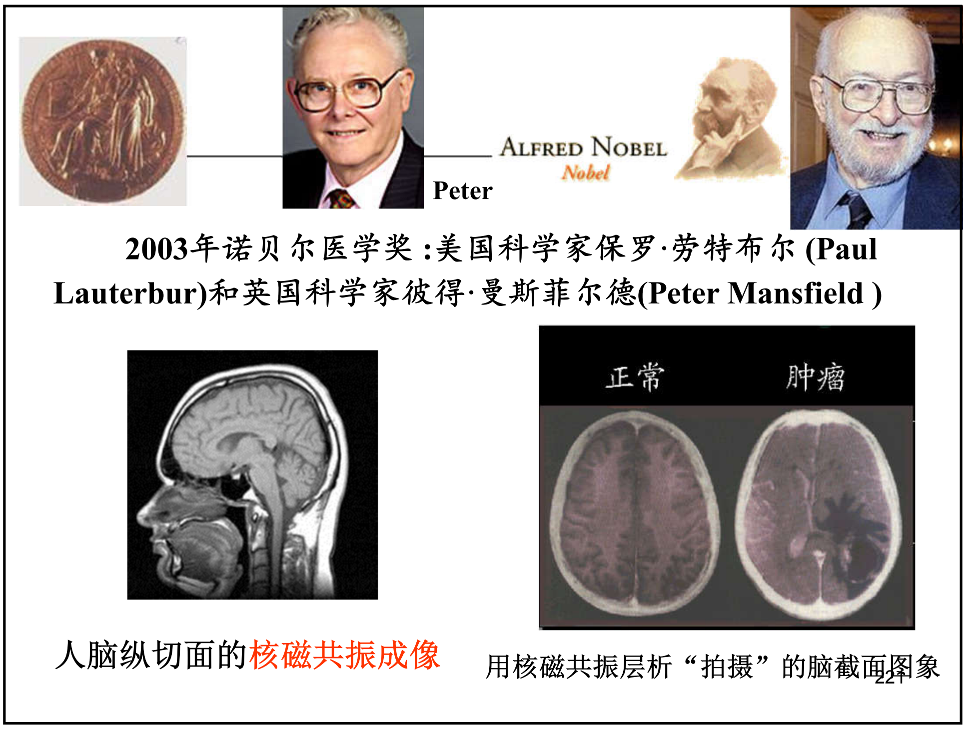
Kurt Wiithrich

2002诺贝尔化学奖:

瑞士科学家库尔特·. 维特里希 “for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution". 他将获得2002年诺贝尔化学奖另一半的奖金。



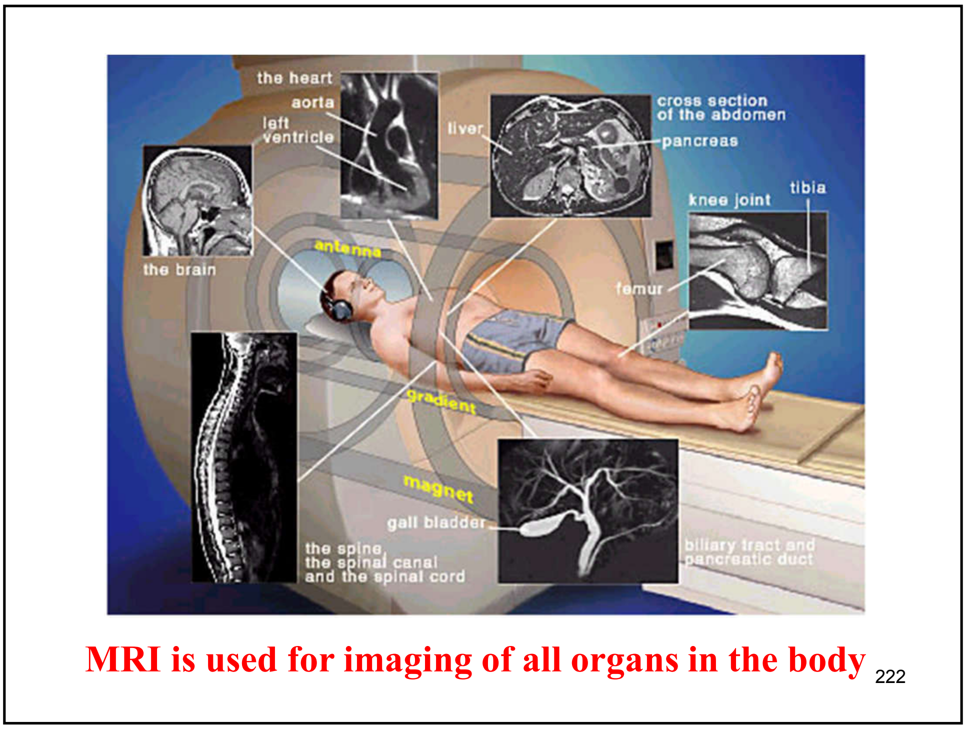
If one knows all the measurements of a house one can draw a three-dimensional picture of that house. In the same way, by measuring a vast number of short distances in a protein, it is possible to create a three-dimensional picture of that protein.



2003年诺贝尔医学奖：美国科学家保罗·劳特布尔 (Paul Lauterbur)和英国科学家彼得·曼斯菲尔德(Peter Mansfield)

人脑纵切面的核磁共振成像

用核磁共振层析“拍摄”的脑截面图象



MRI is used for imaging of all organs in the body

NMR

- (a) The instrument is available in most laboratories;
- (b) An in-depth understanding of the fundamentals of the method is not necessary to apply this method;
- (c) Only a small amount of sample is needed, and this can be recovered;
- (d) Because the analysis is conducted in solution.

- Sensitivity and resolution of NMR spectrometers have been greatly improved by the use of superconducting magnets that can operate at field resonance of up to 1 GHz

梁 晓 天

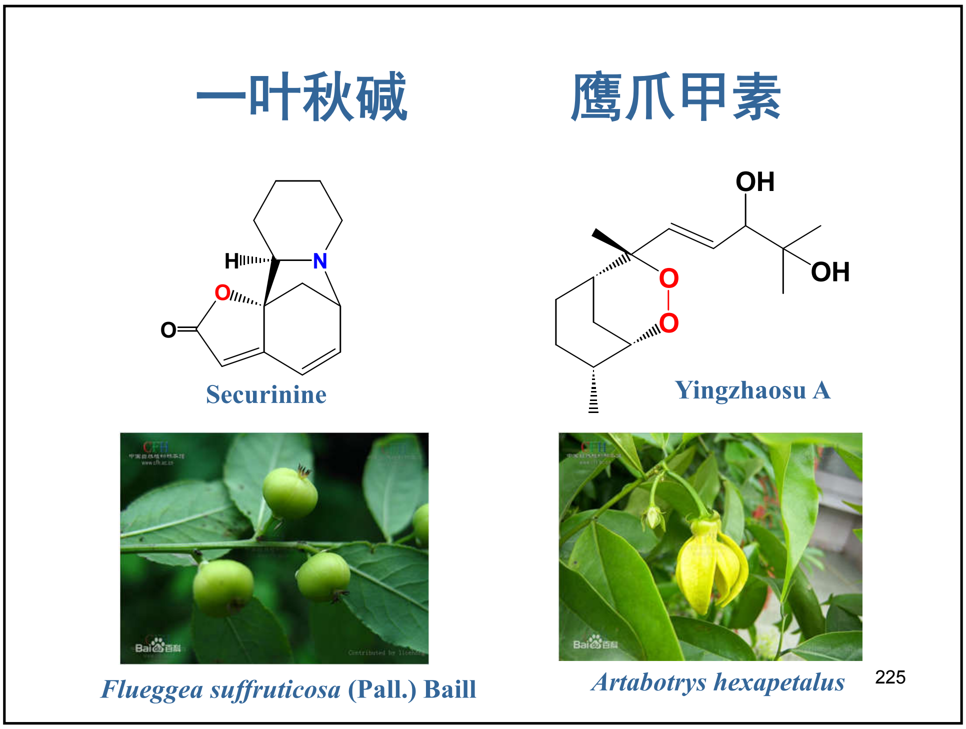
中国核磁共振技術的開拓者

《核磁共振光谱解释简编》
《核磁共振高分辨氢谱的解析和应用》

1923.7-2009.9

一叶秋碱、川楝素、鹤草粉、鹰爪甲素及乙素、创新霉素、亮菌甲素、芍药新苷、海南粗榧、杜鹃素以及一些二萜生物碱等数十个天然产物的结构鉴定。

梁晓天 于德泉 吴伟良 邓槐春 《化学学报》 1979年03期



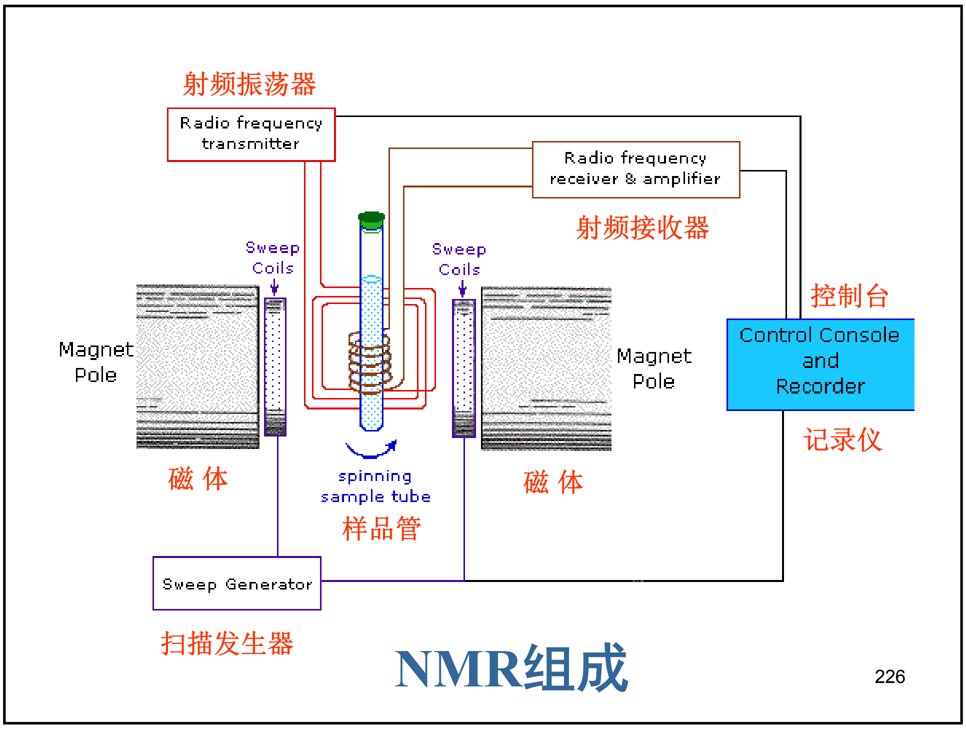
一叶秋碱　　鹰爪甲素

Securinine

Yingzhaosu A

Flueggea suffruticosa **(Pall.) Baill**

Artabotrys hexapetalus



NMR组成

Varian 600 MHz

NMR Spectrometer

Liquid Helium-cooled Magnet


VARIAN
BRUKER
950 US²

NMR Magnets

JEOL RESONANCE 500
JEOL RESONANCE 600
JEOL RESONANCE 700
JEOL RESONANCE 800

Instrument	Stray Magnetic Field (0.5^{m}T line)		Ceiling Height* (m)	Liquid Helium** Refill Period (days)
	Horizontal Direction (m)	Vertical Direction (m)		
400 MHz YH	0.5	1.0	2.84	≥365
500 MHz	0.6	1.15	2.87	≥150
600 MHz	0.7	1.4	3.12	≥200
700 MHz	0.8	1.6	3.12	≥150
800 MHz	1.5	2.5	3.52	≥150

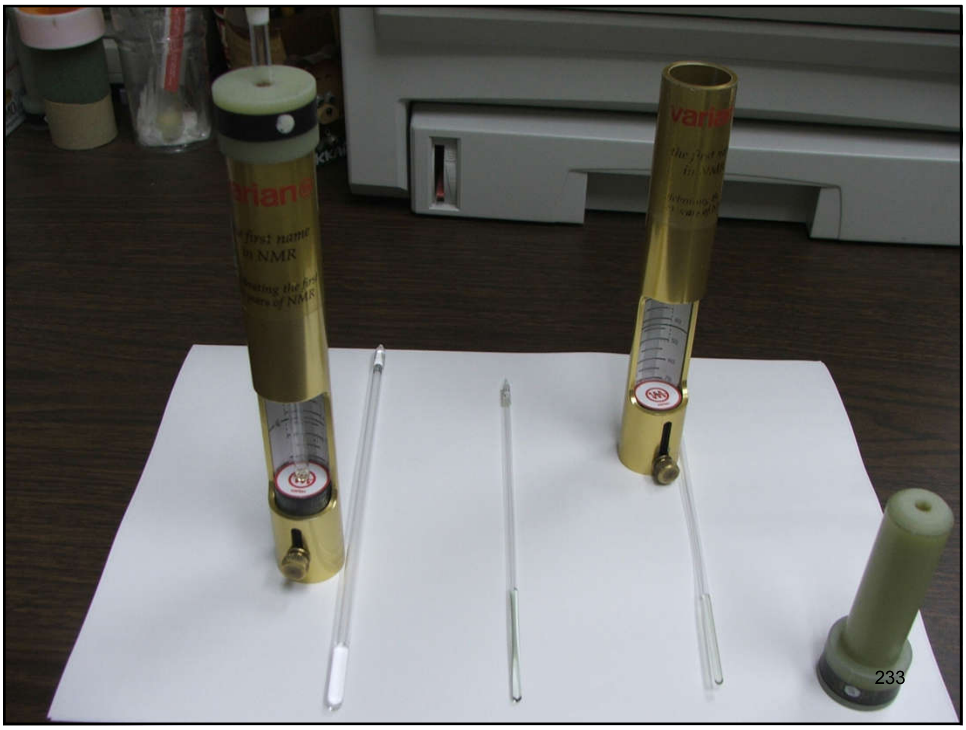
* The required ceiling height ＝ Total height + Current lead length or Transfer tube length

** These values are calculated from the filled capacity and the estimated evaporation rate, the actual number of days may vary depending on the actual use environment.

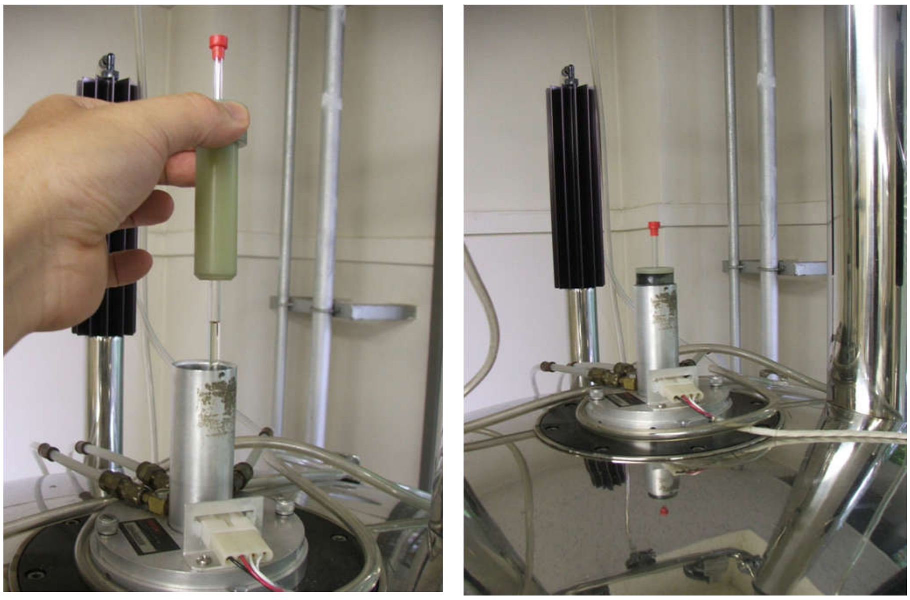
* These values are when the option is used.

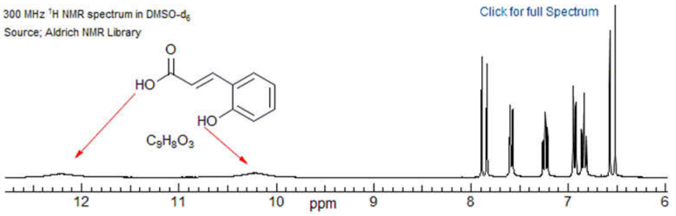
The external appearance and specifications are subject to change without prior notice.

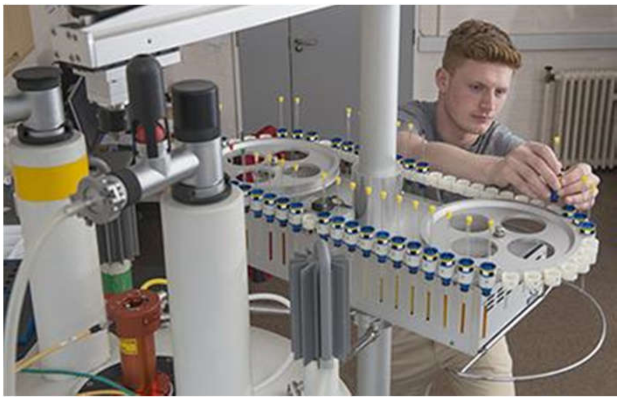
1000兆超导核磁共振波谱仪


varian
the first name in NMR
Celebrating the first 50 years of NMR
233


varian
the first name in NMR
Celebrating the first 50 years of NMR
234




300 MHz ^{1}H NMR spectrum in DMSO-d_6
Source; Aldrich NMR Library
Click for full Spectrum
O
HO
HO
$C_9H_8O_3$
12
11
10
ppm
9
8
7
6



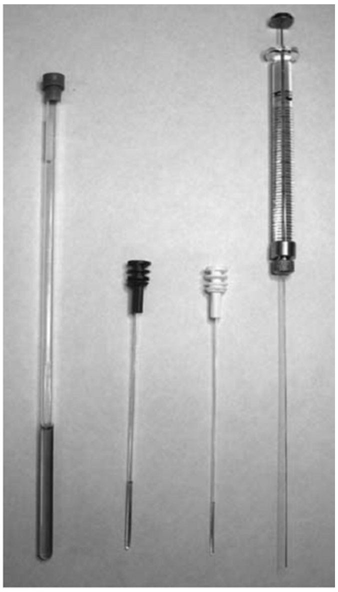
What we can learn from NMR spectra

Chemical Shift: Information about the composition of atomic groups within the molecule.

Spin-Spin coupling constant: Information about adjacent atoms.

Relaxation time: Information on molecular dynamics.

Signal Intensity: Quantitative information, e.g. atomic ratios within a molecule that can be helpful in determining the molecular structure, and proportions of different compounds in a mixture.



5 mm (600 μL),
1.7 mm (35 μL) and
1 mm tubes (7 μL).
Right, a gas-tight sample syringe fitted with an extra long needle. Image credit: D. S. Dalisay.

Fig. 1 Relative NMR sample tube diameter (OD) and sample volumes. From left to right,

Tadeusz F. Molinski. NMR of natural products at the ‘nanomole-scale’. *Nat. Prod. Rep* **2010**, *27*, 321-329.

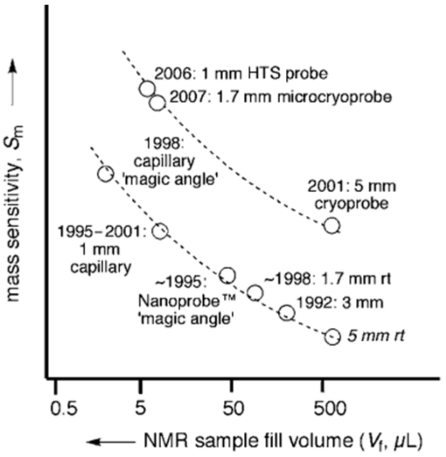
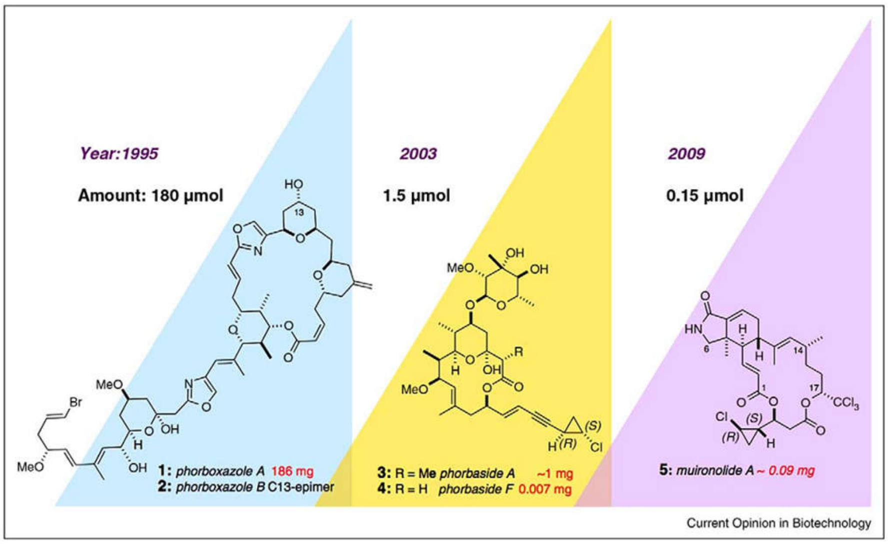


Fig. 2 Approximate time-line and qualitative comparison of recent milestone NMR probe innovations. Mass sensitivity (Sm, linear 'y' scale) for ^{1}H NMR of a hypothetical fixed-mass sample as a function of probe fill volume (Vf, note the logarithmic 'x' scale) for room temperature probes (red line) and cryoprobes (blue line) at fixed field, *B*o. See text for key references. Nanoprobe^{TM} is a trademark of Varian Inc.



Molinski TF. Microscale methodology for structure elucidation of natural products. Curr Opin Biotechnol. 2010; 21:819–826.

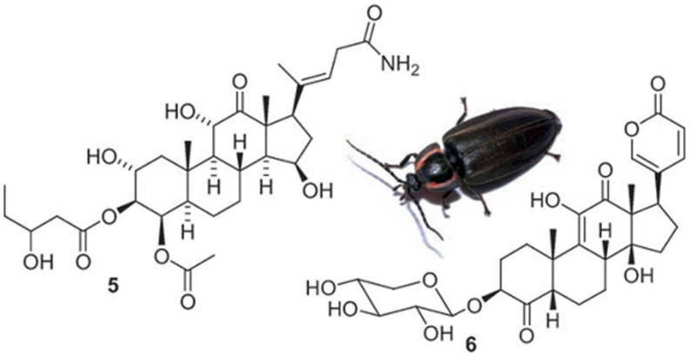
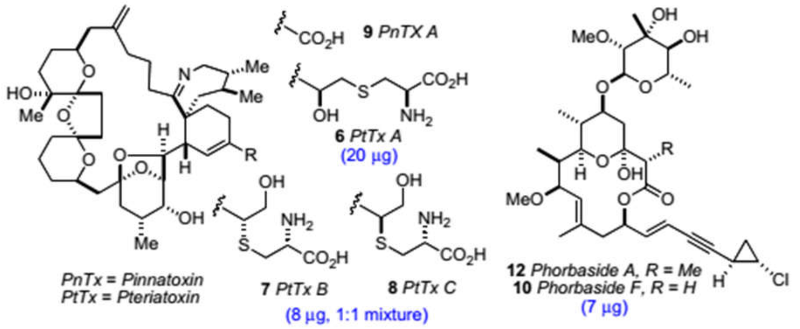


Figure 5. Steroids identified from *Lucidota atra* (一种稀有萤火虫) fireflies by using CapNMRspectroscopy.

Nongradient HMBC spectra of sufficient quality for structure determination were obtained for samples containing as little as 40 nmol of material.

Current generation 1 mm and 1.7 mm microcryoprobe NMR spectrometers allow the acquisition of conventional 2D NMR data with as little sample as a few nanomole.



Tadeusz F. Molinski, Brandon I. Morinaka. Integrated approaches to the configurational assignment of marine natural products. Tetrahedron 68 (2012) 9307-9343.

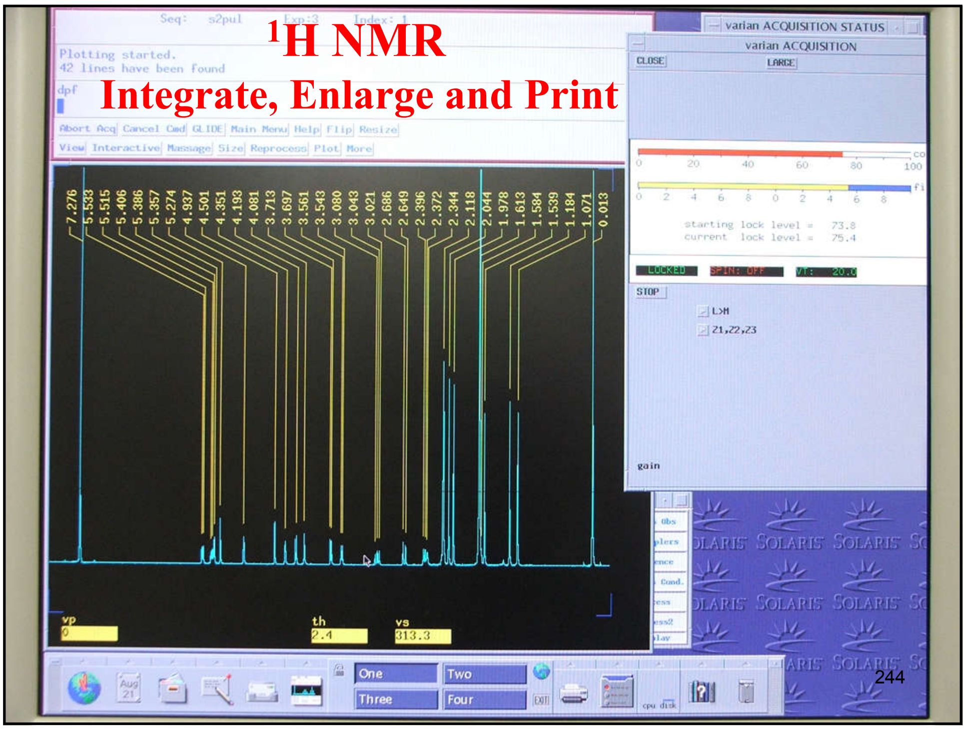
核磁共振波谱分析法的特点及应用范围

(1) NMR是化合物分子结构分析的最重要方法之一。尤其适用于不能获得单晶的化合物或液体（包括溶液中）的化合物的构型、构象的结构分析。

(2) 灵敏度比较低。一般常规要用mg以上的试样作测试，很少作定量分析。定量分析精确度、准确度较差。但国外药典已经应用真伪和杂质的检查。

(3) 在化学反应动力学方面有独特的应用。可用于研究分子内部基团的运动（内旋转），测定反应速度常数，也可以监视一些化学反应的进行过程。

(4) NMR spectra are capable of supplying information about molecular interactions in solution. When a drug interacts with a receptor in a reversible manner, a number of effects may be observed in the spectra due to the exchange of the molecules between free and bound states.



^{1}H NMR

Integrate, Enlarge and Print

Plotting started.
42 lines have been found

NMR

NMR spectra have been a major tool for the study of both newly synthesized and natural products isolated from Nature since 1950s. In the 1980s a second revolution occurred. The introduction of reliable superconducting magnets combined with newly developed, highly sophisticated pulse techniques and the associated Fourier transformation provided the chemist with a method suitable to determine the 3-dimensional structure of very large molecules, *e.g.* biomacromolecules.

Principles

The NMR experiment makes the direct observation of atoms possible. The integral of an NMR signal is strictly linear by proportional to the amount of atoms in the probe volume. The signals are a measure of molar ratios of molecules, independent of the molecular weight.

NMR Spectrum

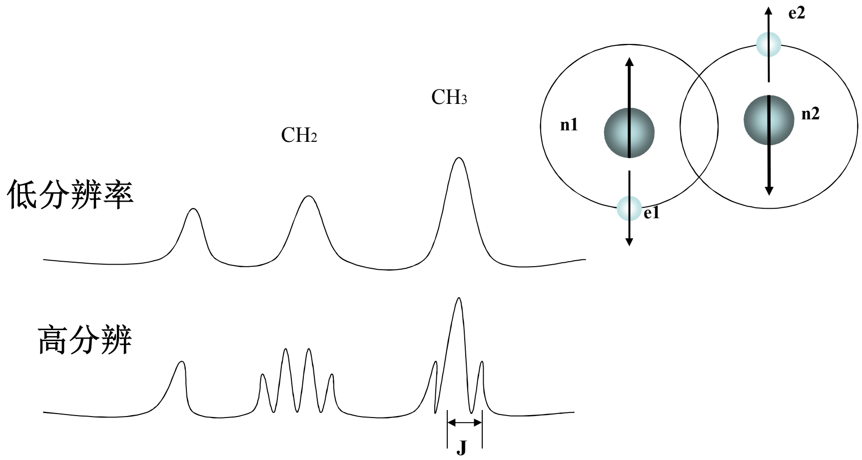
Compared to conventional methods, NMR offers several advantages. It is a non-destructive and reproducible technique, which can be applied to samples of the order of few milligrams in their native form, and performed in a reasonable time without degradation or chemical modification.

Disadvantage

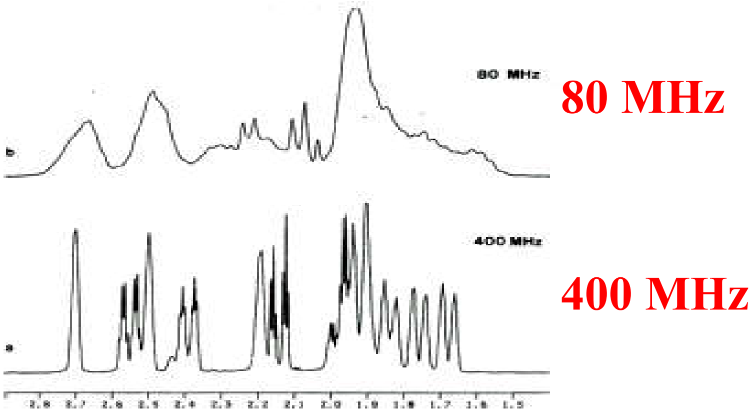
An obvious limitation of NMR technique, however, concerns the determination of absolute configuration which must be achieved by conventional procedures.

NMR is awesome except when H/C is less than 0.7.

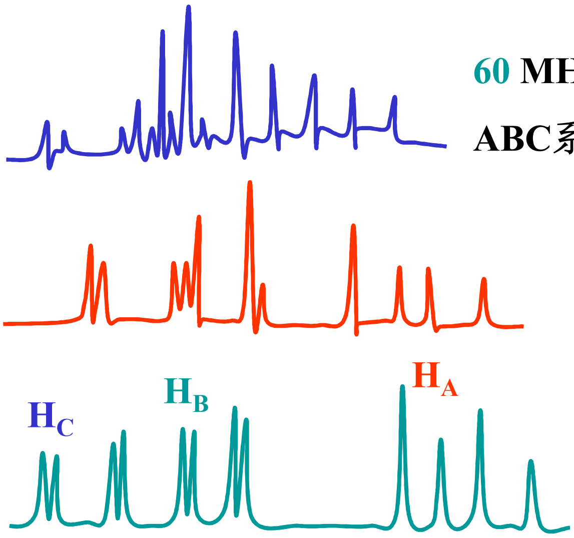
自旋偶合现象



Resolution *vs* Instrument Frequency

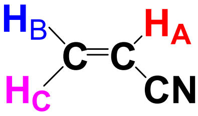


简化谱图的方法–采用高场强仪器



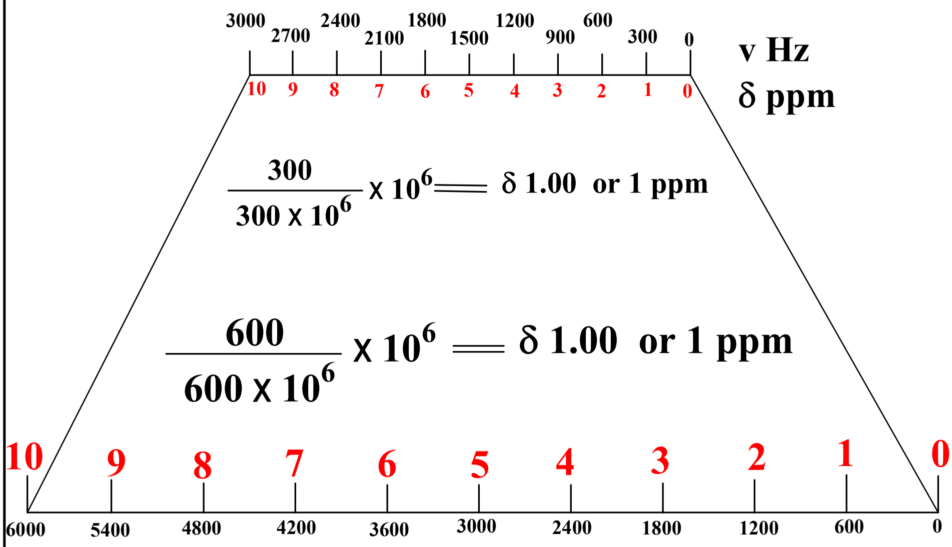
60 MHz

ABC系统



- 100 MHz
- ABX系统

- 220 MHz
- AMX系统



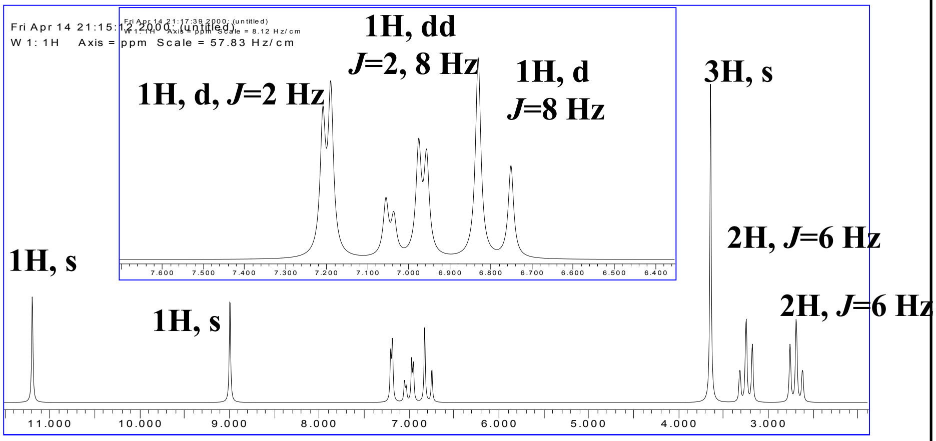
v Hz

δ ppm

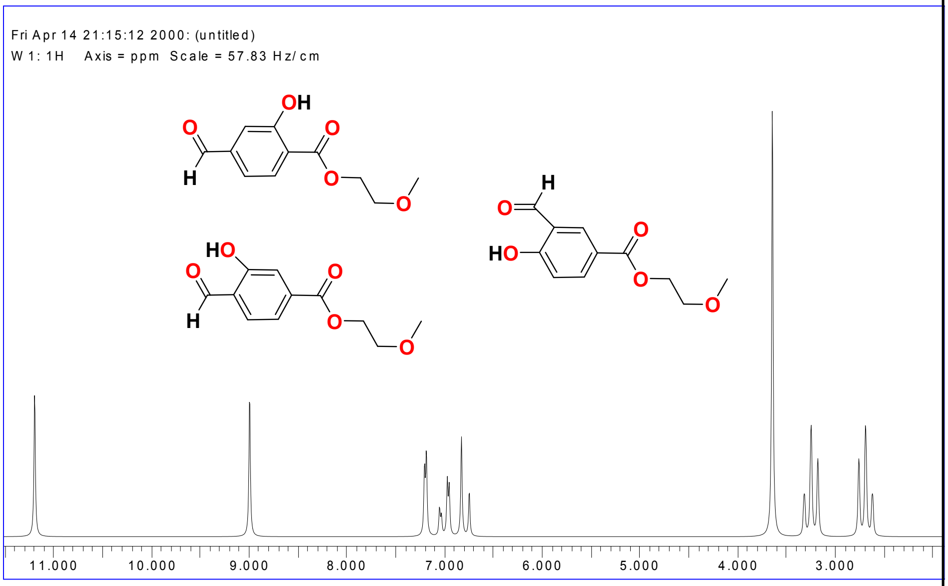
$$\frac{300}{300 \times 10^6} \times 10^6 = \delta\ 1.00 \text{ or } 1 \text{ ppm}$$

$$\frac{600}{600 \times 10^6} \times 10^6 = \delta\ 1.00 \text{ or } 1 \text{ ppm}$$

$C_{11}H_{12}O_5$ 的^{1}H-NMR谱如下，推导其可能的结构



ABX system



Informative NMR Parameters

Chemical shift

Spin-spin splitting

Line widths

The nuclear Overhauser effect

Chemical exchange.

自旋-自旋偶合

自旋核与自旋核之间的相互作用（干扰）

偶合的结果 造成谱线增多，称之裂分。

偶合的程度用偶合常数（*J*）表示，单位: **Hz**

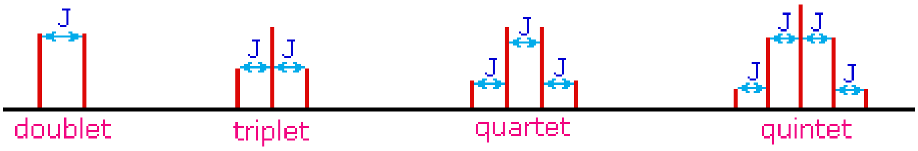
Abbreviations for proton multiplicities:

s = singlet, d = doublet, t = triplet,

q = quartet, m = multiplet.

Higher multiplicities are given in full *i.e.*

quintet, hextet, heptet, *etc.*



NMR Spectrum

The X-axis of the spectrum is called the delta scale (δ) with units of ppm and the Y-axis is an intensity scale. The height of the peak on the Y-axis is proportional to the number of ^{1}H nuclei in the molecule with the same chemical shift.

δ is a ratio of Hz/MHz, the result is a ratio without units (1/1 x 10^6) or one over one million. A better term for "one over one millionth" is parts-per-million or ppm.

乙 醇

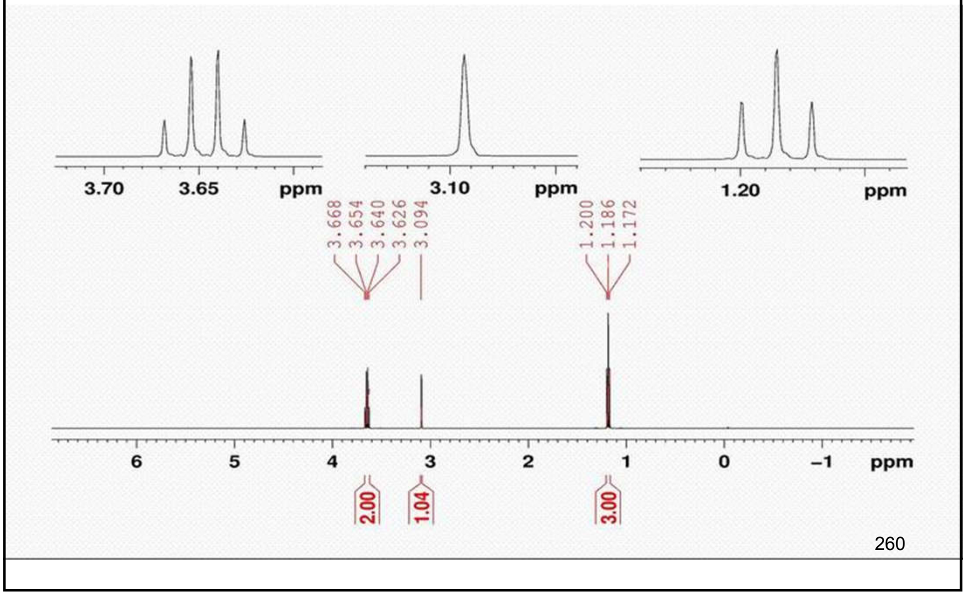
1951年Arnold首先发现乙醇的NMR信号及与结构的关系。

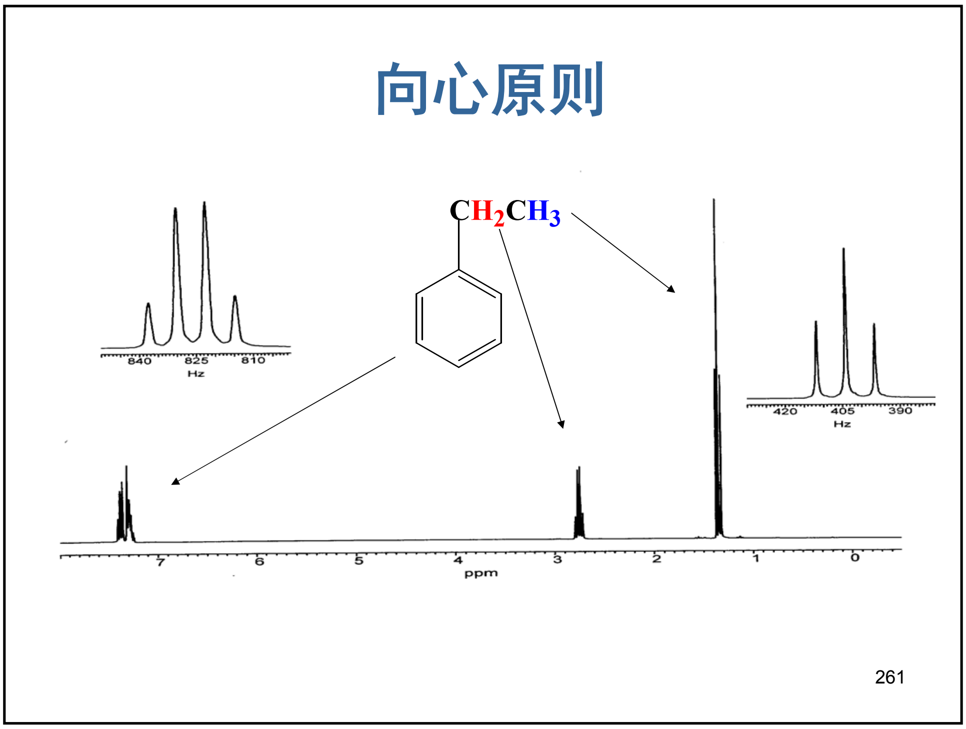
向心原则 $HOCH_2CH_3$

In 1951, the proton spectrum of ethanol with three distinct resonances showed the potential of NMR for structure elucidation of organic compounds.

---

^{1}H-NMR of ethanol (CH_3CH_2OH)





向心原则

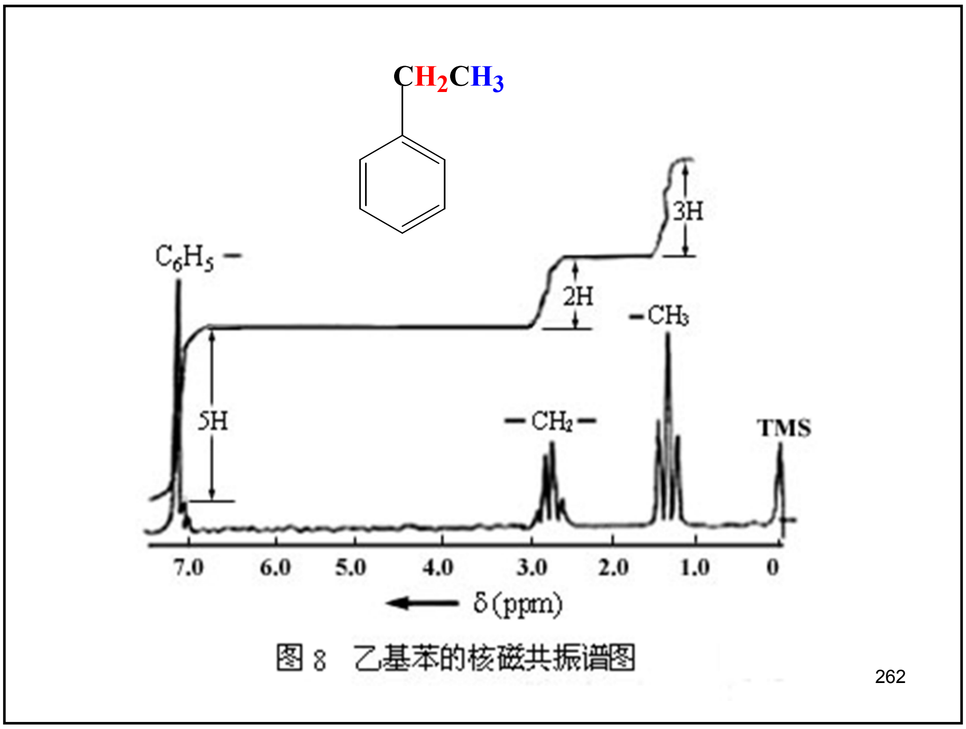
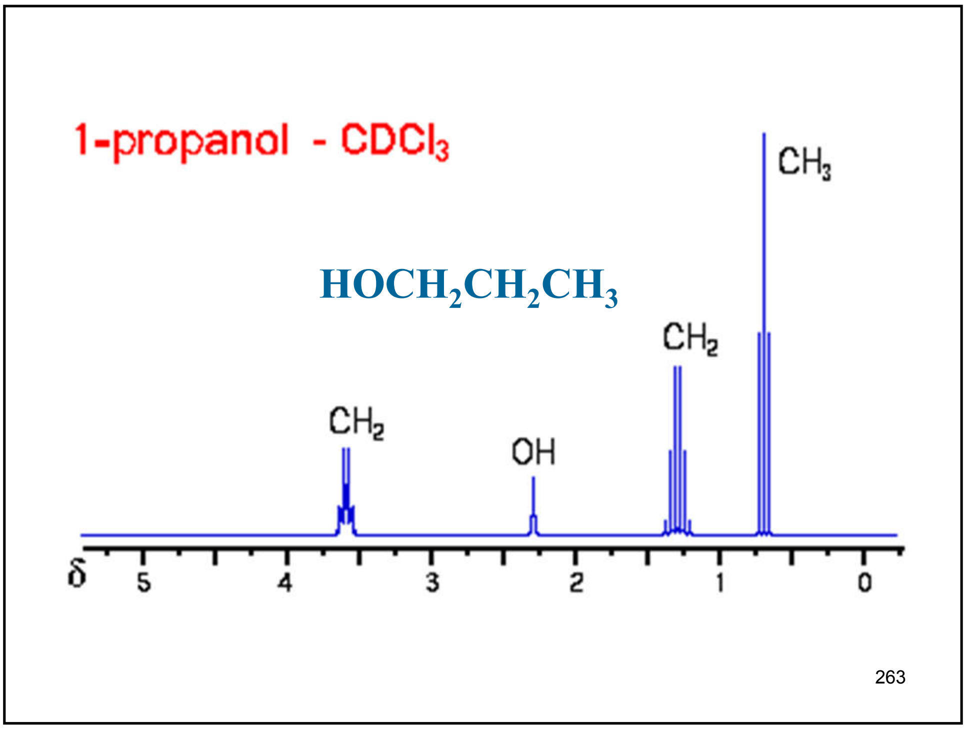


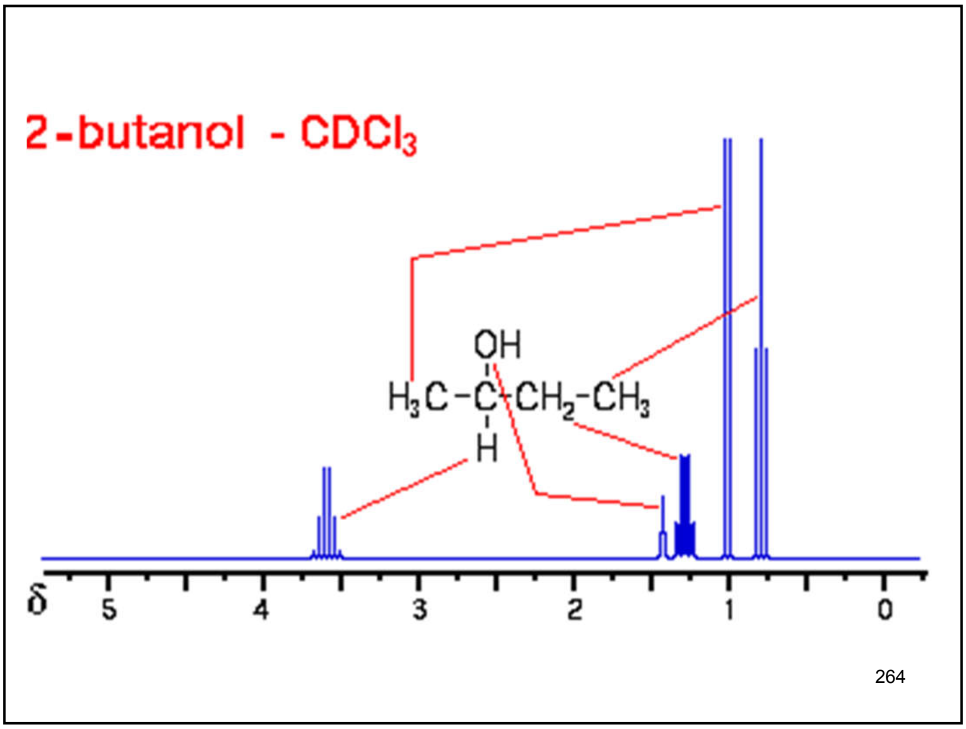
图 8　乙基苯的核磁共振谱图



1-propanol - $CDCl_3$

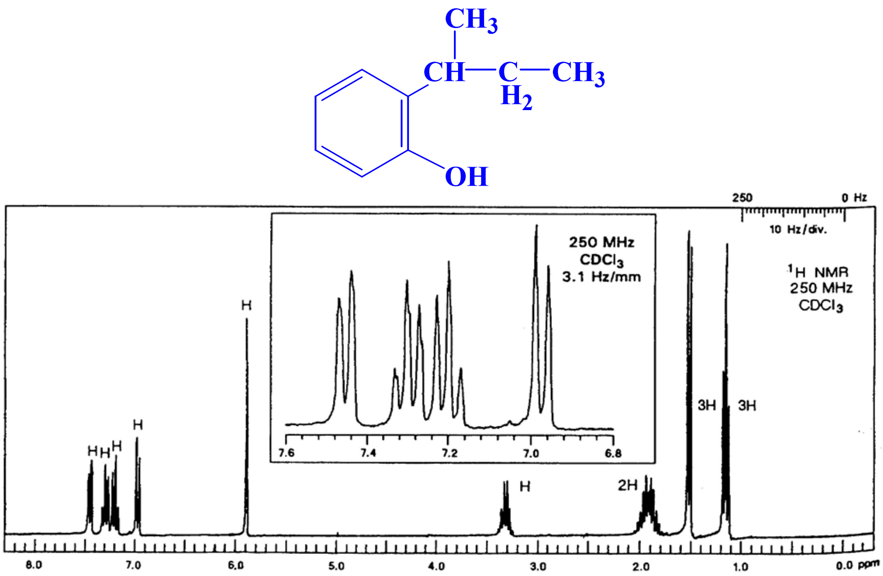
$HOCH_2CH_2CH_3$

263



2-butanol - $CDCl_3$

264



Chemical Shift

The frequency of absorption for a nucleus of interest relative to the frequency of absorption of a molecular standard is called the Chemical Shift of the nucleus. The molecular standard for both ^{1}H and ^{13}C-NMR spectroscopy is (TMS) tetramethylsilane. Because of molecular symmetry all 12 protons of TMS absorb at the same frequency and all 4 carbons absorb at the same frequency.

NMR Solvents

Most NMR spectra are recorded for compounds dissolved in a solvent. Therefore, signals will be observed for the solvent and this must be accounted for in solving spectral problems.

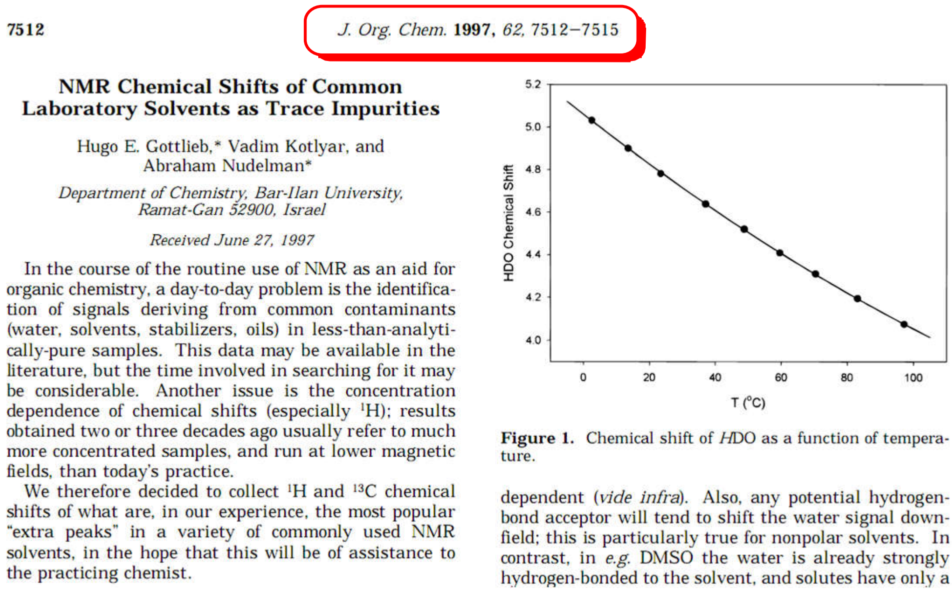
H. E. Gottlieb, V. Kotylar, A. Nudelman, **^{1}H-NMR Data of solvents and impurities.** *J. Org. Chem*. **1997**, *62*: 7512-7515.

NMR Solvents

To avoid spectra dominated by the solvent signal, most ^{1}H-NMR spectra are recorded in a *deuterated* solvent. However, DEUTERATION IS NOT "100%", so signals for the residual protons are observed. In *deuterated* chloroform solvent ($CDCl_3$), this corresponds to $CHCl_3$, so a singlet signal is observed at d 7.26 ppm.

NMR Solvent Signals

	^{1}H	^{13}C
Acetone	2.05	206.7, 29.9
Acetonitrile	1.94	118.7, 1.39
Benzene	7.16	128.4
Chloroform	7.26	77.2
Methanol	4.87, 3.31	49.1
Pyridine	8.74, 7.58,7.22	150.3,135.9, 123.9
Water (D_2O)	4.8	



7512 *J. Org. Chem.* **1997,** *62,* 7512–7515

NMR Chemical Shifts of Common Laboratory Solvents as Trace Impurities

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Received June 27, 1997

In the course of the routine use of NMR as an aid for organic chemistry, a day-to-day problem is the identification of signals deriving from common contaminants (water, solvents, stabilizers, oils) in less-than-analytically-pure samples. This data may be available in the literature, but the time involved in searching for it may be considerable. Another issue is the concentration dependence of chemical shifts (especially ^{1}H); results obtained two or three decades ago usually refer to much more concentrated samples, and run at lower magnetic fields, than today's practice.

We therefore decided to collect ^{1}H and ^{13}C chemical shifts of what are, in our experience, the most popular "extra peaks" in a variety of commonly used NMR solvents, in the hope that this will be of assistance to the practicing chemist.

Figure 1. Chemical shift of *H*DO as a function of temperature.

dependent (*vide infra*). Also, any potential hydrogen-bond acceptor will tend to shift the water signal downfield; this is particularly true for nonpolar solvents. In contrast, in *e.g.* DMSO the water is already strongly hydrogen-bonded to the solvent, and solutes have only a

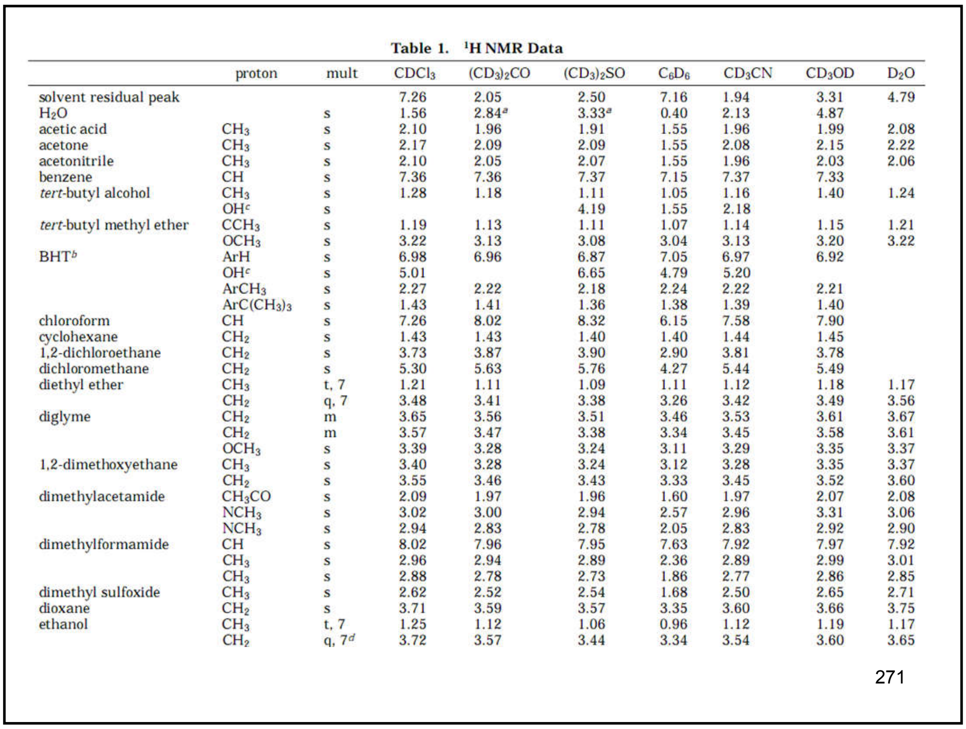


Table 1. ¹H NMR Data

	proton	mult	$CDCl_3$	$(CD_3)_2CO$	$(CD_3)_2SO$	C_6D_6	CD_3CN	CD_3OD	D_2O
solvent residual peak			7.26	2.05	2.50	7.16	1.94	3.31	4.79
H_2O		s	1.56	2.84[a]	3.33[a]	0.40	2.13	4.87	
acetic acid	CH_3	s	2.10	1.96	1.91	1.55	1.96	1.99	2.08
acetone	CH_3	s	2.17	2.09	2.09	1.55	2.08	2.15	2.22
acetonitrile	CH_3	s	2.10	2.05	2.07	1.55	1.96	2.03	2.06
benzene	CH	s	7.36	7.36	7.37	7.15	7.37	7.33	
tert-butyl alcohol	CH_3	s	1.28	1.18	1.11	1.05	1.16	1.40	1.24
	OH[c]	s			4.19	1.55	2.18		
tert-butyl methyl ether	CCH_3	s	1.19	1.13	1.11	1.07	1.14	1.15	1.21
	OCH_3	s	3.22	3.13	3.08	3.04	3.13	3.20	3.22
BHT[b]	ArH	s	6.98	6.96	6.87	7.05	6.97	6.92	
	OH[c]	s	5.01		6.65	4.79	5.20		
	$ArCH_3$	s	2.27	2.22	2.18	2.24	2.22	2.21	
	$ArC(CH_3)_3$	s	1.43	1.41	1.36	1.38	1.39	1.40	
chloroform	CH	s	7.26	8.02	8.32	6.15	7.58	7.90	
cyclohexane	CH_2	s	1.43	1.43	1.40	1.40	1.44	1.45	
1,2-dichloroethane	CH_2	s	3.73	3.87	3.90	2.90	3.81	3.78	
dichloromethane	CH_2	s	5.30	5.63	5.76	4.27	5.44	5.49	
diethyl ether	CH_3	t, 7	1.21	1.11	1.09	1.11	1.12	1.18	1.17
	CH_2	q, 7	3.48	3.41	3.38	3.26	3.42	3.49	3.56
diglyme	CH_2	m	3.65	3.56	3.51	3.46	3.53	3.61	3.67
	CH_2	m	3.57	3.47	3.38	3.34	3.45	3.58	3.61
	OCH_3	s	3.39	3.28	3.24	3.11	3.29	3.35	3.37
1,2-dimethoxyethane	CH_3	s	3.40	3.28	3.24	3.12	3.28	3.35	3.37
	CH_2	s	3.55	3.46	3.43	3.33	3.45	3.52	3.60
dimethylacetamide	CH_3CO	s	2.09	1.97	1.96	1.60	1.97	2.07	2.08
	NCH_3	s	3.02	3.00	2.94	2.57	2.96	3.31	3.06
	NCH_3	s	2.94	2.83	2.78	2.05	2.83	2.92	2.90
dimethylformamide	CH	s	8.02	7.96	7.95	7.63	7.92	7.97	7.92
	CH_3	s	2.96	2.94	2.89	2.36	2.89	2.99	3.01
	CH_3	s	2.88	2.78	2.73	1.86	2.77	2.86	2.85
dimethyl sulfoxide	CH_3	s	2.62	2.52	2.54	1.68	2.50	2.65	2.71
dioxane	CH_2	s	3.71	3.59	3.57	3.35	3.60	3.66	3.75
ethanol	CH_3	t, 7	1.25	1.12	1.06	0.96	1.12	1.19	1.17
	CH_2	q, 7[d]	3.72	3.57	3.44	3.34	3.54	3.60	3.65

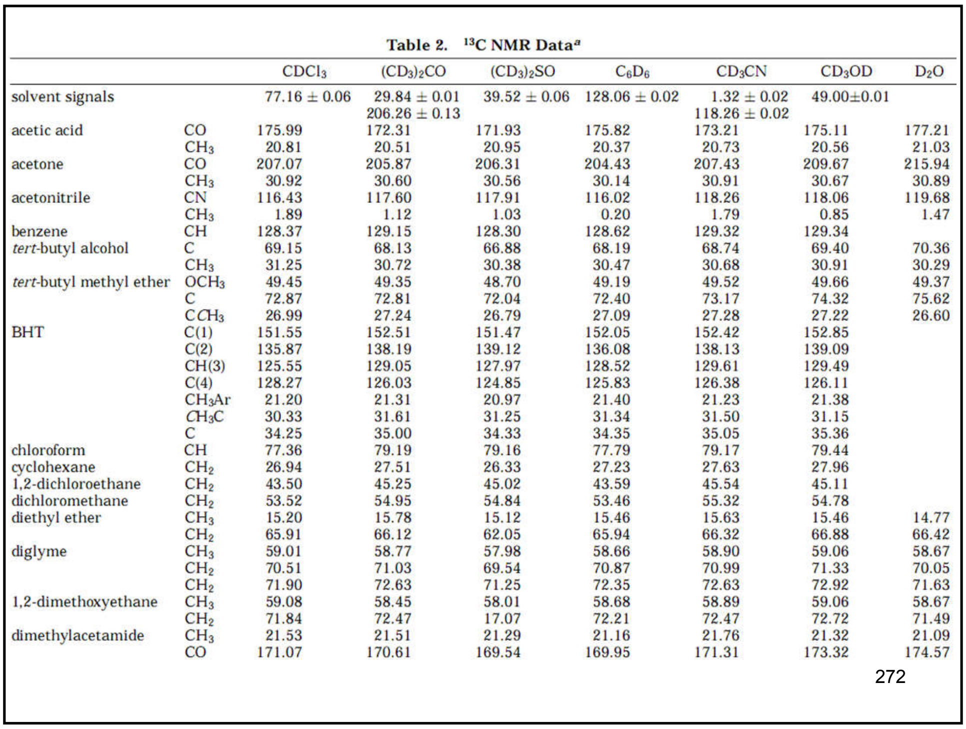
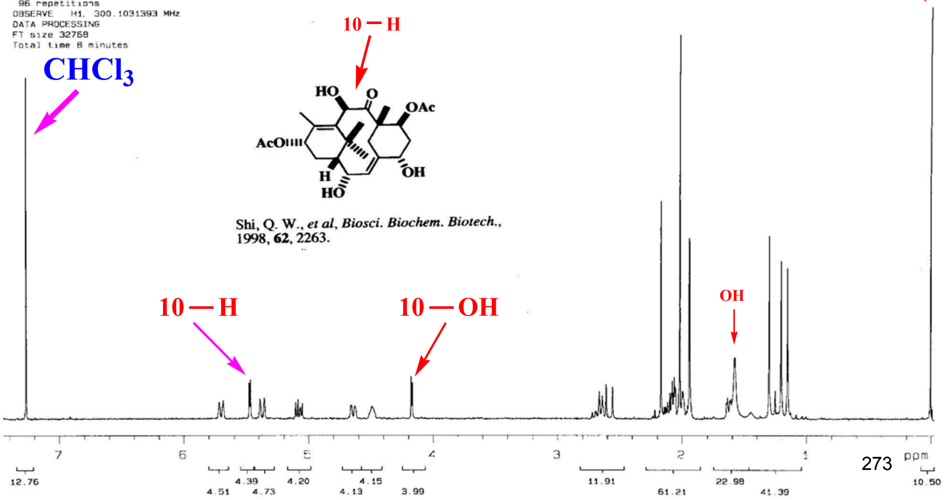


Table 2. ¹³C NMR Data[a]

		$CDCl_3$	$(CD_3)_2CO$	$(CD_3)_2SO$	C_6D_6	CD_3CN	CD_3OD	D_2O
solvent signals		77.16 ± 0.06	29.84 ± 0.01 206.26 ± 0.13	39.52 ± 0.06	128.06 ± 0.02	1.32 ± 0.02 118.26 ± 0.02	49.00±0.01	
acetic acid	CO	175.99	172.31	171.93	175.82	173.21	175.11	177.21
	CH_3	20.81	20.51	20.95	20.37	20.73	20.56	21.03
acetone	CO	207.07	205.87	206.31	204.43	207.43	209.67	215.94
	CH_3	30.92	30.60	30.56	30.14	30.91	30.67	30.89
acetonitrile	CN	116.43	117.60	117.91	116.02	118.26	118.06	119.68
	CH_3	1.89	1.12	1.03	0.20	1.79	0.85	1.47
benzene	CH	128.37	129.15	128.30	128.62	129.32	129.34	
tert-butyl alcohol	C	69.15	68.13	66.88	68.19	68.74	69.40	70.36
	CH_3	31.25	30.72	30.38	30.47	30.68	30.91	30.29
tert-butyl methyl ether	OCH_3	49.45	49.35	48.70	49.19	49.52	49.66	49.37
	C	72.87	72.81	72.04	72.40	73.17	74.32	75.62
	$C\mathit{CH}_3$	26.99	27.24	26.79	27.09	27.28	27.22	26.60
BHT	C(1)	151.55	152.51	151.47	152.05	152.42	152.85	
	C(2)	135.87	138.19	139.12	136.08	138.13	139.09	
	CH(3)	125.55	129.05	127.97	128.52	129.61	129.49	
	C(4)	128.27	126.03	124.85	125.83	126.38	126.11	
	CH_3Ar	21.20	21.31	20.97	21.40	21.23	21.38	
	CH_3C	30.33	31.61	31.25	31.34	31.50	31.15	
	C	34.25	35.00	34.33	34.35	35.05	35.36	
chloroform	CH	77.36	79.19	79.16	77.79	79.17	79.44	
cyclohexane	CH_2	26.94	27.51	26.33	27.23	27.63	27.96	
1,2-dichloroethane	CH_2	43.50	45.25	45.02	43.59	45.54	45.11	
dichloromethane	CH_2	53.52	54.95	54.84	53.46	55.32	54.78	
diethyl ether	CH_3	15.20	15.78	15.12	15.46	15.63	15.46	14.77
	CH_2	65.91	66.12	62.05	65.94	66.32	66.88	66.42
diglyme	CH_3	59.01	58.77	57.98	58.66	58.90	59.06	58.67
	CH_2	70.51	71.03	69.54	70.87	70.99	71.33	70.05
	CH_2	71.90	72.63	71.25	72.35	72.63	72.92	71.63
1,2-dimethoxyethane	CH_3	59.08	58.45	58.01	58.68	58.89	59.06	58.67
	CH_2	71.84	72.47	17.07	72.21	72.47	72.72	71.49
dimethylacetamide	CH_3	21.53	21.51	21.29	21.16	21.76	21.32	21.09
	CO	171.07	170.61	169.54	169.95	171.31	173.32	174.57

^{1}H-NMR Spectrum

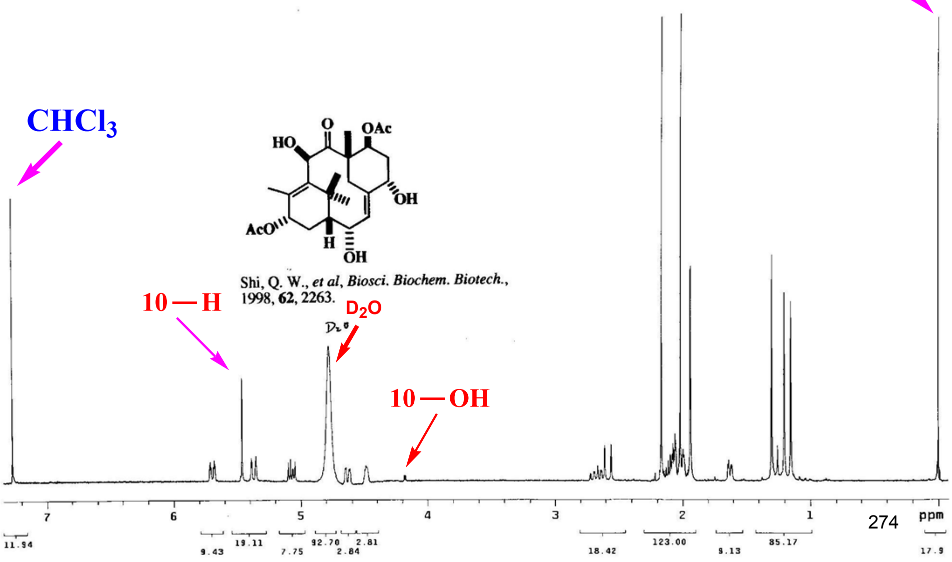
```
5/15-11-shi
 Date: Apr  4 98
 Solvent: CDCl3
 Ambient temperature
GEMINI-300  "varian"
PULSE SEQUENCE
 Relax. delay 1.502 sec
 Pulse 45.2 degrees
 Acq. time 3.498 sec
 Width 4500.5 Hz
 96 repetitions
OBSERVE   H1, 300.1031393 MHz
DATA PROCESSING
FT size 32768
Total time 8 minutes
```



Shi, Q. W., *et al*, *Biosci. Biochem. Biotech.*, 1998, **62**, 2263.

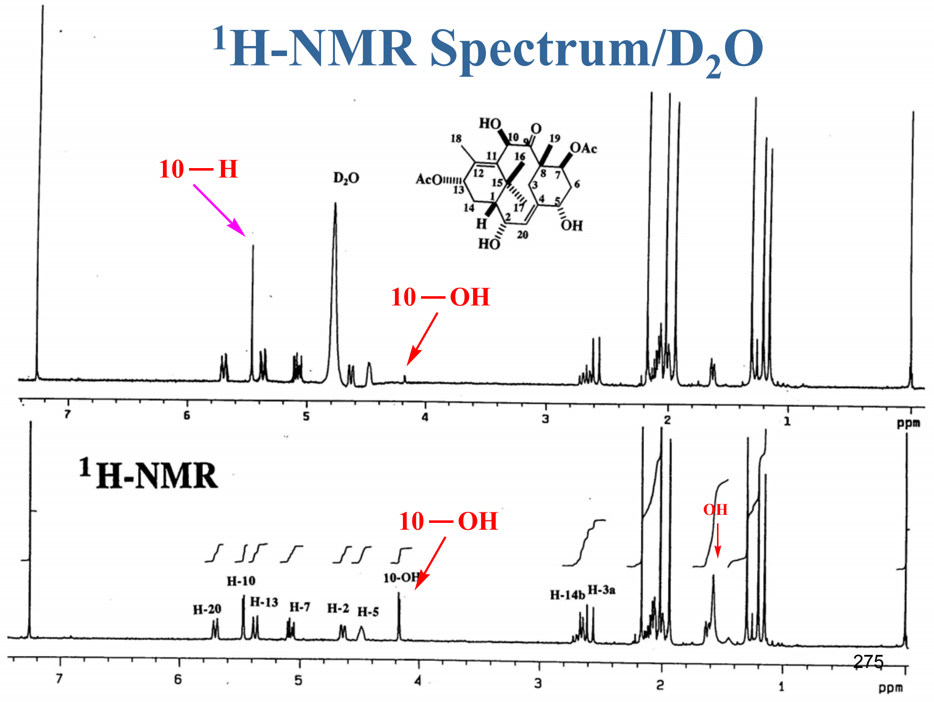
^{1}H-NMR Spectrum + D_2O

```
5/15-11-shi-D2O
 Date: May 15 98
 Solvent: CDCl3
 Ambient temperature
GEMINI-300  "varian"
PULSE SEQUENCE
 Relax. delay 1.502 sec
 Pulse 45.2 degrees
 Acq. time 3.498 sec
 Width 4500.5 Hz
 48 repetitions
OBSERVE   H1, 300.1031388 MHz
DATA PROCESSING
FT size 32768
Total time 4 minutes
```



Shi, Q. W., *et al*, *Biosci. Biochem. Biotech.*, 1998, **62**, 2263.

^{1}H-NMR Spectrum/D_2O



TMS

在化学位移测定时，常用的标准物是四甲基硅烷（$(CH_3)_4Si$，简称 **TMS**。**TMS** 用作标准物质的优点是：

1. **TMS** 化学性质不活泼，与样品之间不发生化学反应和分子间缔合；
2. **TMS** 是一个对称结构，四个甲基有相同的化学环境，因此无论在氢谱还是在碳谱中都只有一个吸收峰；
3. 因为 **Si**的电负性（**1.9**）比 **C** 的电负性（**2.5**）小，**TMS** 中的氢核和碳核处在高电子密度区，产生大的屏蔽效应，它产生 **NMR** 信号所需的磁场强度比一般有机物中的氢核和碳核产生 **NMR** 信号所需的磁场强度都大得多，与绝大部分样品信号之间不会互相重叠干扰；
4. **TMS** 沸点很低（**27**度），容易去除，有利于回收样品。
5. 但 **TMS** 是非极性溶剂，不溶于水。对于那些强极性试样，必须用重水为溶剂测谱时要用其它标准物。

TMS

It used to be common practice to add Me_4Si, or related compounds, as an internal reference standard for ^1H and ^{13}C NMR spectra with the proton signal occurring at 0.0 ppm and the carbon signal occurring at 0.0 ppm in the ^{13}C NMR spectrum. However, modern spectrometers can "lock" on solvent signals, so addition of internal reference standards is not usually required.

$CDCl_3$, 7.26 ppm for H and 77.7 ppm for C.

In the NMR spectrum of an organic compound, peaks appear at the positions of absorption, also called the *positions of resonance* or *precession frequencies*, for different nuclei in the molecule. The exact chemical shift of a particular nucleus in a molecule gives us information about how the atom with that nucleus is bonded in the molecule.

化学位移

- 在^{1}H 谱和^{13}C 谱中都规定标准物 TMS 的化学位移值 δ = 0，位于图谱的右边。在它的左边 δ 为正值，在它的右边 δ为负值，绝大部分有机物中的氢核或碳核的化学位移都是正值。
- 当外磁场强度自左至右扫描逐渐增大时，δ值却自左至右逐渐减小。
- 凡是 δ 值较小的核，就说它处于高场。
- 不同的同位素核因屏蔽常数变化幅度不等， δ值变化的幅度也不同，如^{1}H 的 δ值小于 20，^{13}C 的 δ大部分在 0-250，而^{195}Pt的 δ 可达 13000。

Chemical shift

Chemical shift **is defined as *nuclear shielding / applied magnetic field.***

Chemical shift is a function of the nucleus and its environment.

化学位移的表示法

- **1.** 用赫兹(Hz, CPS)表示化学位移(现已不用)。
- **2.** 用δ值表示　δ值的定义:

$$\delta = \frac{\upsilon_{样} - \upsilon_{标}}{\upsilon_{标}} \times 10^{6} = \frac{\triangle\upsilon}{振荡器射频} \times 10^{6}$$

用τ表示时，**TMS τ = 10 ppm**

早期文献用Hz或CPS表示位移，根据所用仪器的功率，计算一下。

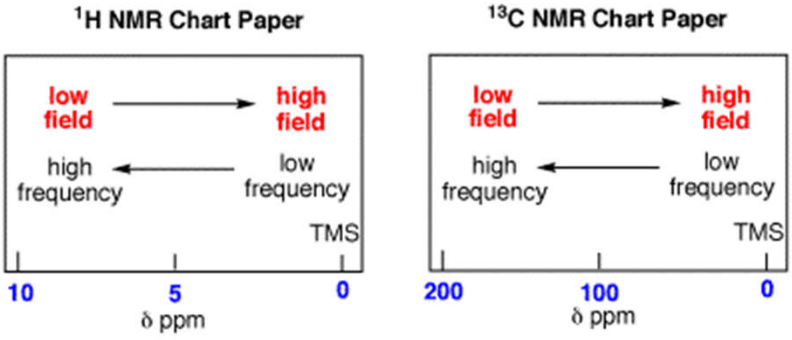
1970年，国际纯粹和应用化学协会(IUPAC)建议化学位移一律采用δ值，并规定TMS左边峰δ值为正，右边峰δ值为负。

如用δ值表示：

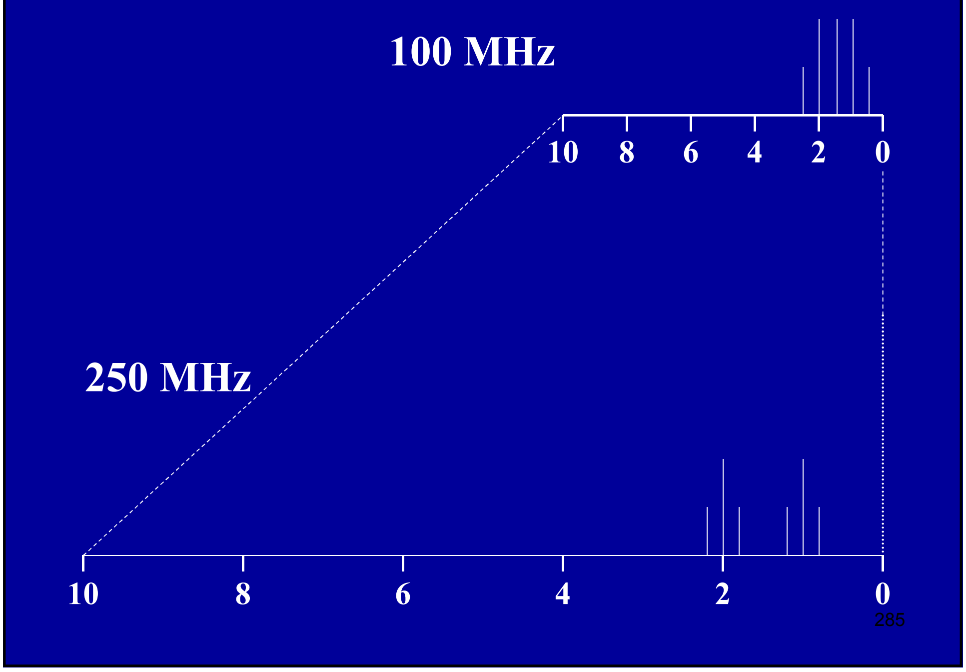
60 MHz $$\delta = \frac{134-0}{60 \times 10^6} \times 10^6 = 2.23\ \text{ppm}$$

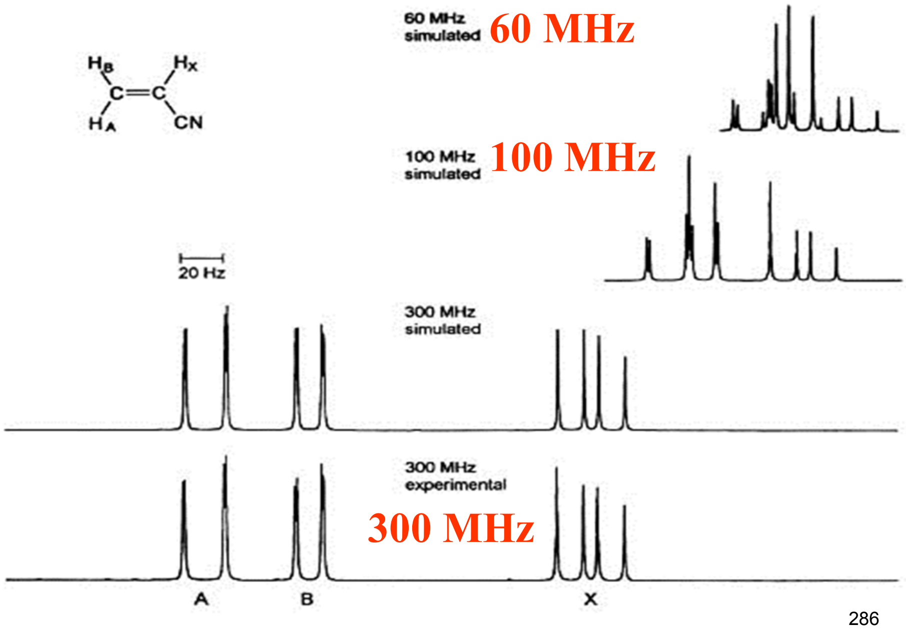
100 MHz $$\delta = \frac{223-0}{100 \times 10^6} \times 10^6 = 2.23\ \text{ppm}$$

Figure 1 . NMR chart papers for ^{1}H and ^{13}C NMR.



Down-field **Up-field**


100 MHz
10
8
6
4
2
0
250 MHz
10
8
6
4
2
0


H_B
H_X
C=C
H_A
CN
60 MHz simulated
60 MHz
100 MHz simulated
100 MHz
20 Hz
300 MHz simulated
300 MHz experimental
300 MHz
A
B
X

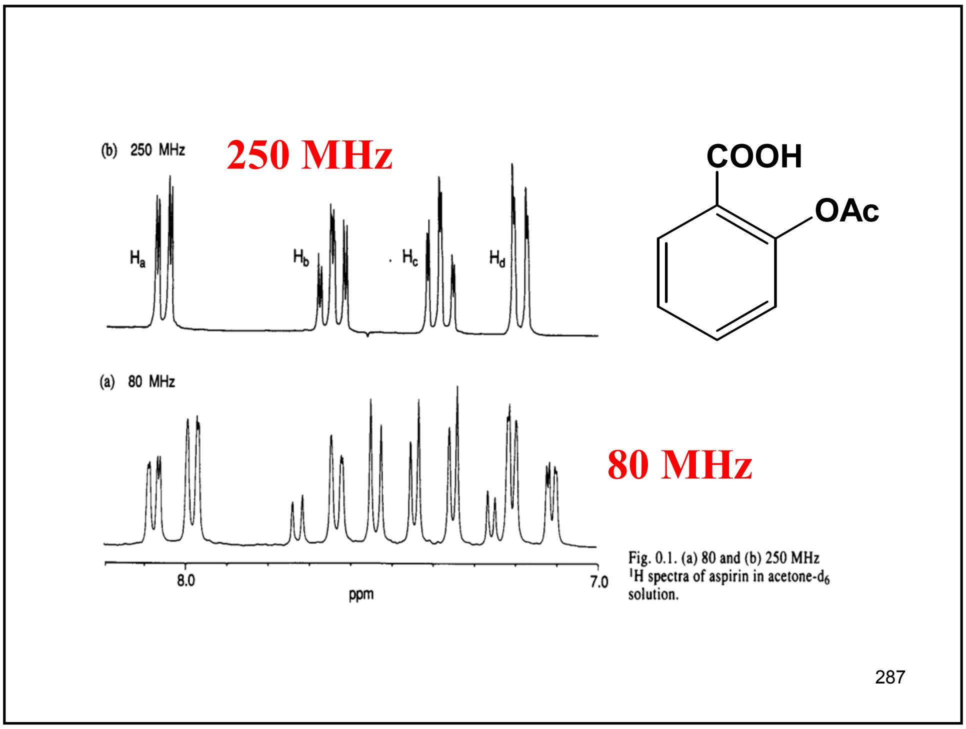
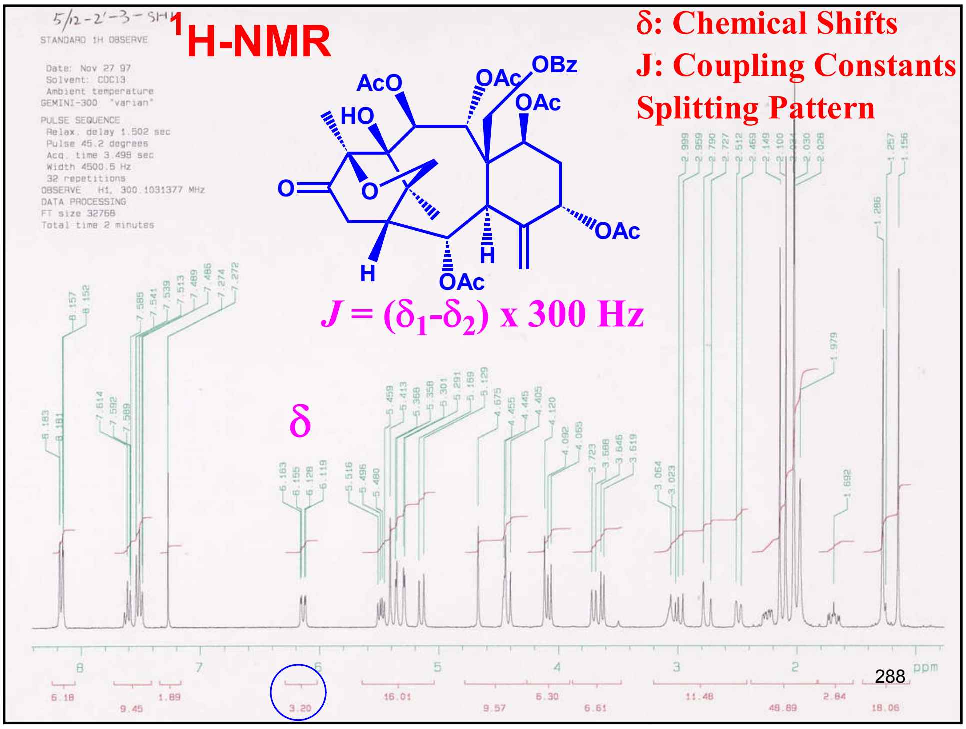


Fig. 0.1. (a) 80 and (b) 250 MHz ^1H spectra of aspirin in acetone-d_6 solution.



5/12-2′-3-SH1

^{1}H-NMR

δ: Chemical Shifts
J: Coupling Constants
Splitting Pattern

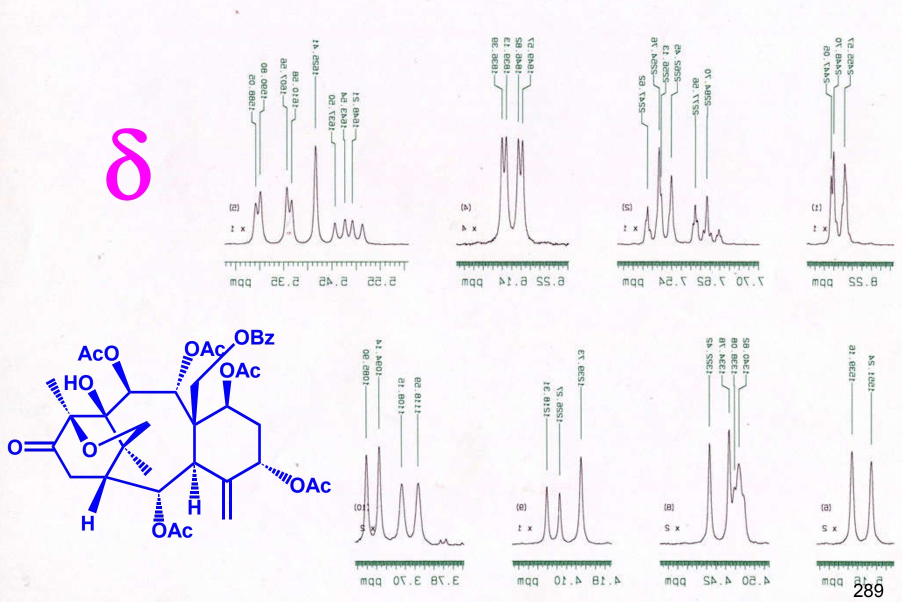
```
STANDARD 1H OBSERVE

 Date: Nov 27 97
 Solvent: CDC13
 Ambient temperature
GEMINI-300  "varian"
PULSE SEQUENCE
 Relax. delay 1.502 sec
 Pulse 45.2 degrees
 Acq. time 3.498 sec
 Width 4500.5 Hz
 32 repetitions
OBSERVE   H1, 300.1031377 MHz
DATA PROCESSING
FT size 32768
Total time 2 minutes
```

$J = (\delta_1 - \delta_2) \times 300$ Hz

$J = (\delta_1-\delta_2) \times 300$ Hz

δ



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^{1}H-NMR图的信息

- **吸收峰的组数**
  - 对一级图谱而言，分子中化学环境不同的质子有几组。
- **质子的化学位移值δ**
  - 说明分子中的基团情况。
- **峰的分裂个数及偶合常数*J***
  - 说明各基团的连接关系。
- **阶梯式积分曲线高度**
  - 说明各基团的质子数比。

Factors Affecting Chemical Shifts

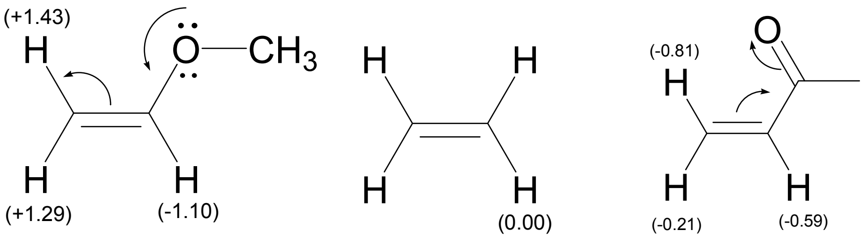
- ● **Substitution and Hybridisation**
- ● **Inductive and Conjugative effects**
- ● **Anisotropic effects**
- ● **Van der Waals force**
- ● **Hydrogen-bonding**
- ● **Solvent effects**

影响化学位移的因素

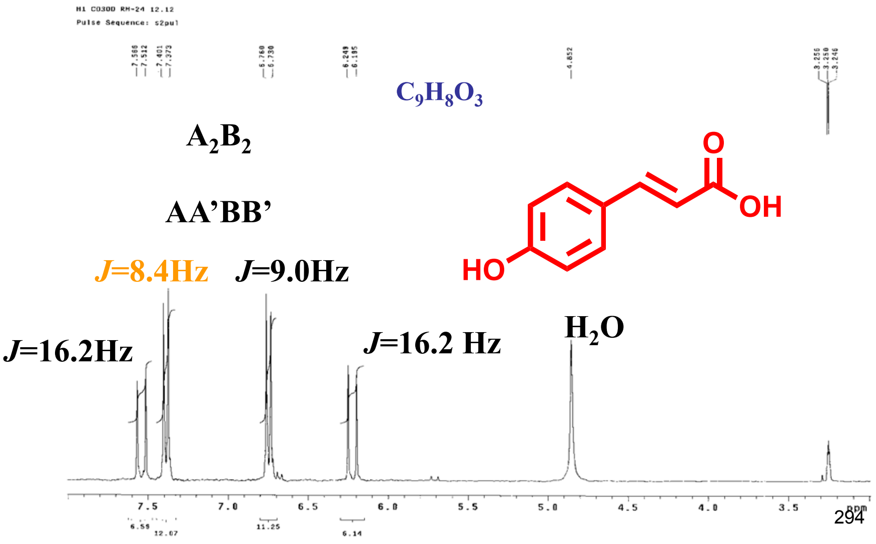
- 氢键的影响： 氢键可以削弱对氢键质子的屏蔽，使共振吸收移向低场。
- 分子内氢键受环境影响较小，所以与样品浓度、温度变化不大；分子间氢键受环境影响较大，当样品浓度、温度发生变化时，氢键质子的化学位移会发生变化。

共轭效应 （conjugative effect）

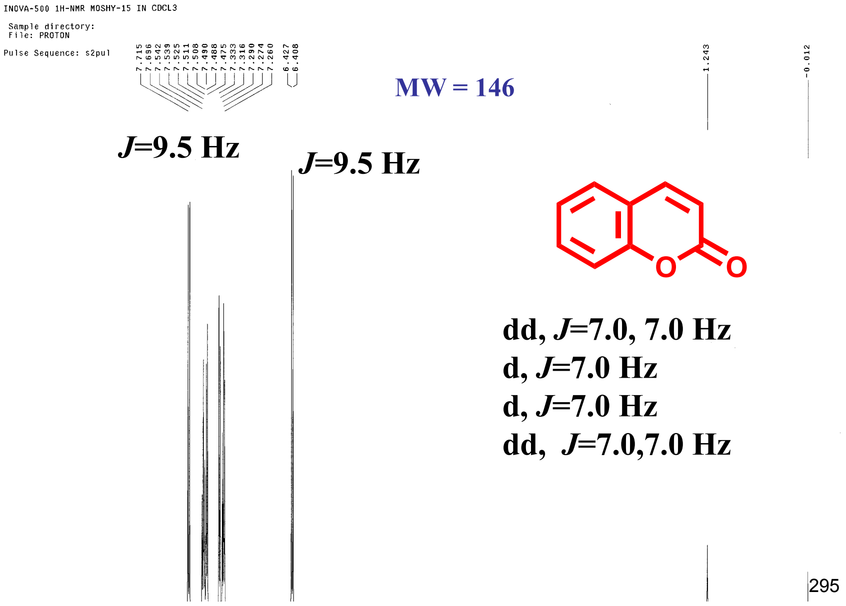
在共轭效应中，推电子基使δ_H减小，拉电子基使δ_H增大。



图谱解析



图谱解析



MW = 146

J=9.5 Hz

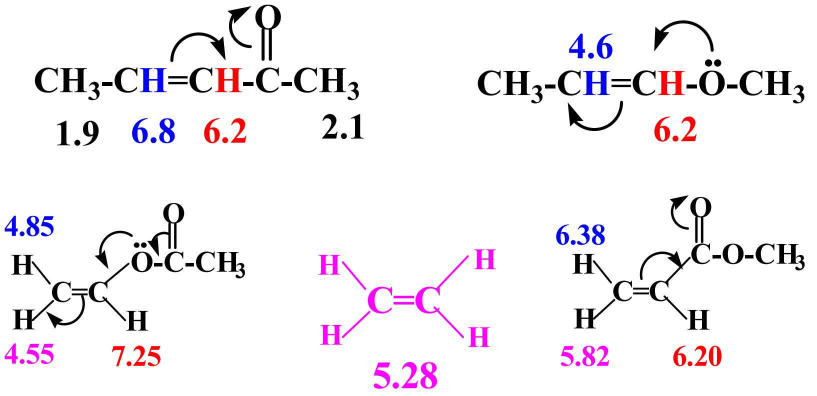
J=9.5 Hz

dd, *J*=7.0, 7.0 Hz
d, *J*=7.0 Hz
d, *J*=7.0 Hz
dd, *J*=7.0,7.0 Hz

共轭效应

- P-π共轭　　π-π共轭

Conjugative Effect : Shielding



影响化学位移的因素

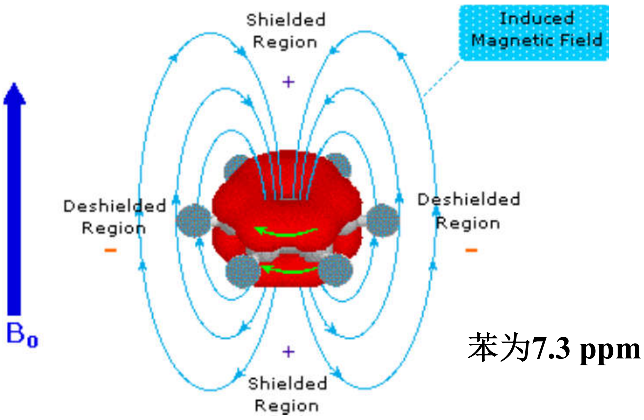
2. 相连碳原子的SP杂化

与H相连的碳原子以SP^3 (碳碳单键)到SP^2 (碳碳 双键)，S电子的成分从25%增加到33%，键电子更靠近碳原子，因而对相连的氢原子有去屏蔽作用，即δ移向低磁场。炔烃的H相当于烯烃处于较高场，则另有原因，下面详述。

影响化学位移的因素

- 3. 环状共轭体系的环电流效应

乙烯的δ值为**5.23 ppm**，苯为**7.3 ppm**，但**C＝C** 均为**SP²**杂化，仅以**SP²**杂化来考虑，苯的δ值应为**5.7 ppm**左右，而实际上更偏低场，这是由于存在着环电流效应，如下图：



苯为**7.3 ppm**

苯环上的氢位于苯环侧面，其环电流产生的磁场方向与外加磁场在苯环的侧面是相同的，即环电流增强了外磁场，氢核被去屏蔽，其共振峰移向较低磁场。