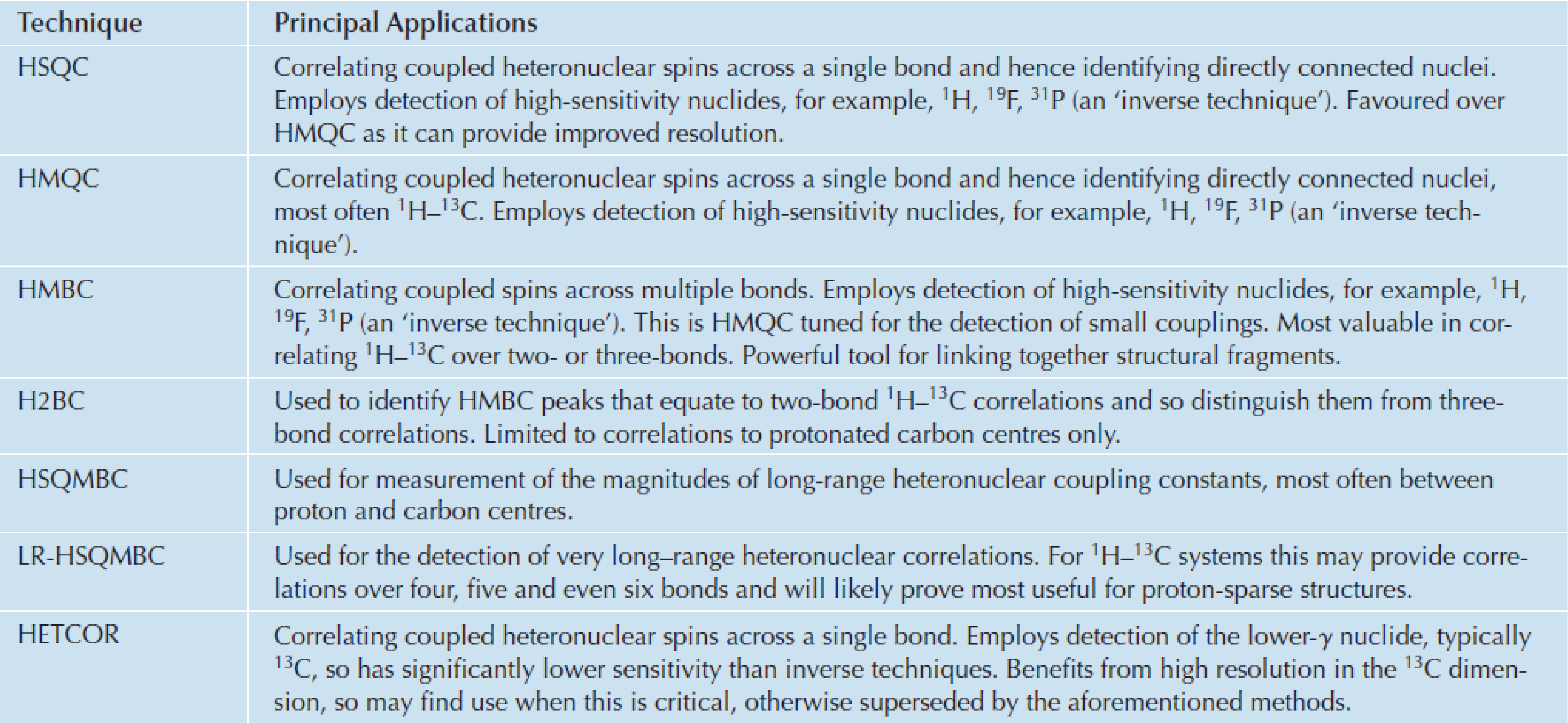
# NMR - 2D

## 2. CORRELAZIONI ETERONUCLEARI
## SHIFT CORRELATE



| | Technique | Principal Applications |
|---|---|---|
| $^1J$ | HSQC | Correlating coupled heteronuclear spins across a single bond and hence identifying directly connected nuclei. Employs detection of high-sensitivity nuclides, for example, $^1H$, $^{19}F$, $^{31}P$ (an 'inverse technique'). Favoured over HMQC as it can provide improved resolution. |
| $^1J$ | HMQC | Correlating coupled heteronuclear spins across a single bond and hence identifying directly connected nuclei, most often $^1H$–$^{13}C$. Employs detection of high-sensitivity nuclides, for example, $^1H$, $^{19}F$, $^{31}P$ (an 'inverse technique'). |
| $^2J$, $^3J$ | HMBC | Correlating coupled spins across multiple bonds. Employs detection of high-sensitivity nuclides, for example, $^1H$, $^{19}F$, $^{31}P$ (an 'inverse technique'). This is HMQC tuned for the detection of small couplings. Most valuable in correlating $^1H$–$^{13}C$ over two- or three-bonds. Powerful tool for linking together structural fragments. |
| $^2J$ | H2BC | Used to identify HMBC peaks that equate to two-bond $^1H$–$^{13}C$ correlations and so distinguish them from three-bond correlations. Limited to correlations to protonated carbon centres only. |
| Long range | HSQMBC | Used for measurement of the magnitudes of long-range heteronuclear coupling constants, most often between proton and carbon centres. |
| Long range | LR-HSQMBC | Used for the detection of very long–range heteronuclear correlations. For $^1H$–$^{13}C$ systems this may provide correlations over four, five and even six bonds and will likely prove most useful for proton-sparse structures. |
| $^1J$ | HETCOR | Correlating coupled heteronuclear spins across a single bond. Employs detection of the lower-$\gamma$ nuclide, typically $^{13}C$, so has significantly lower sensitivity than inverse techniques. Benefits from high resolution in the $^{13}C$ dimension, so may find use when this is critical, otherwise superseded by the aforementioned methods. |

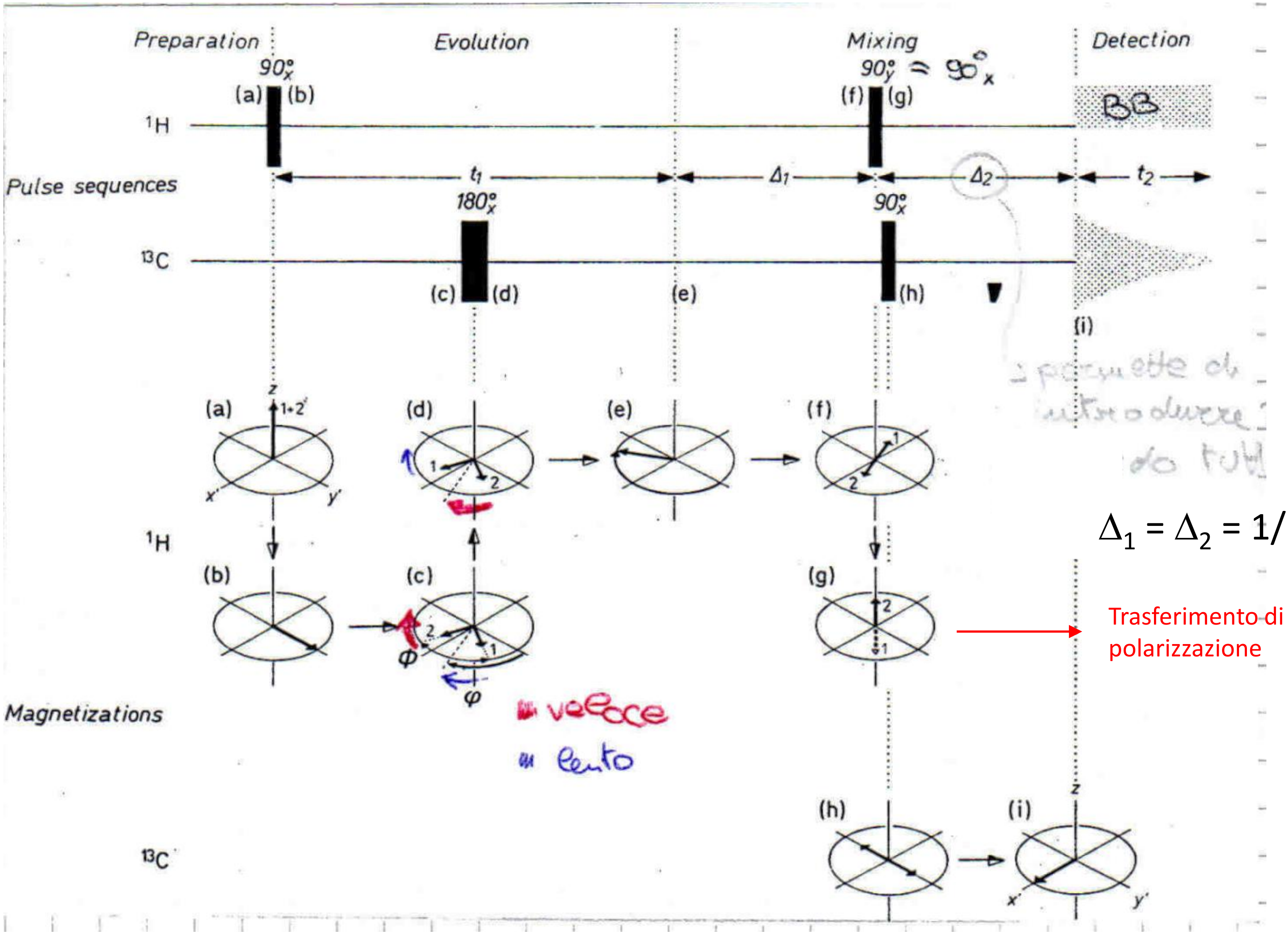
# H,C-COSY
# C,H-COSY

Informazione: quale C è attaccato a quale protone

- Differenza: nel primo caso il nucleo osservato (F2) è il $^{13}$C (poco sensibile) HETCOR

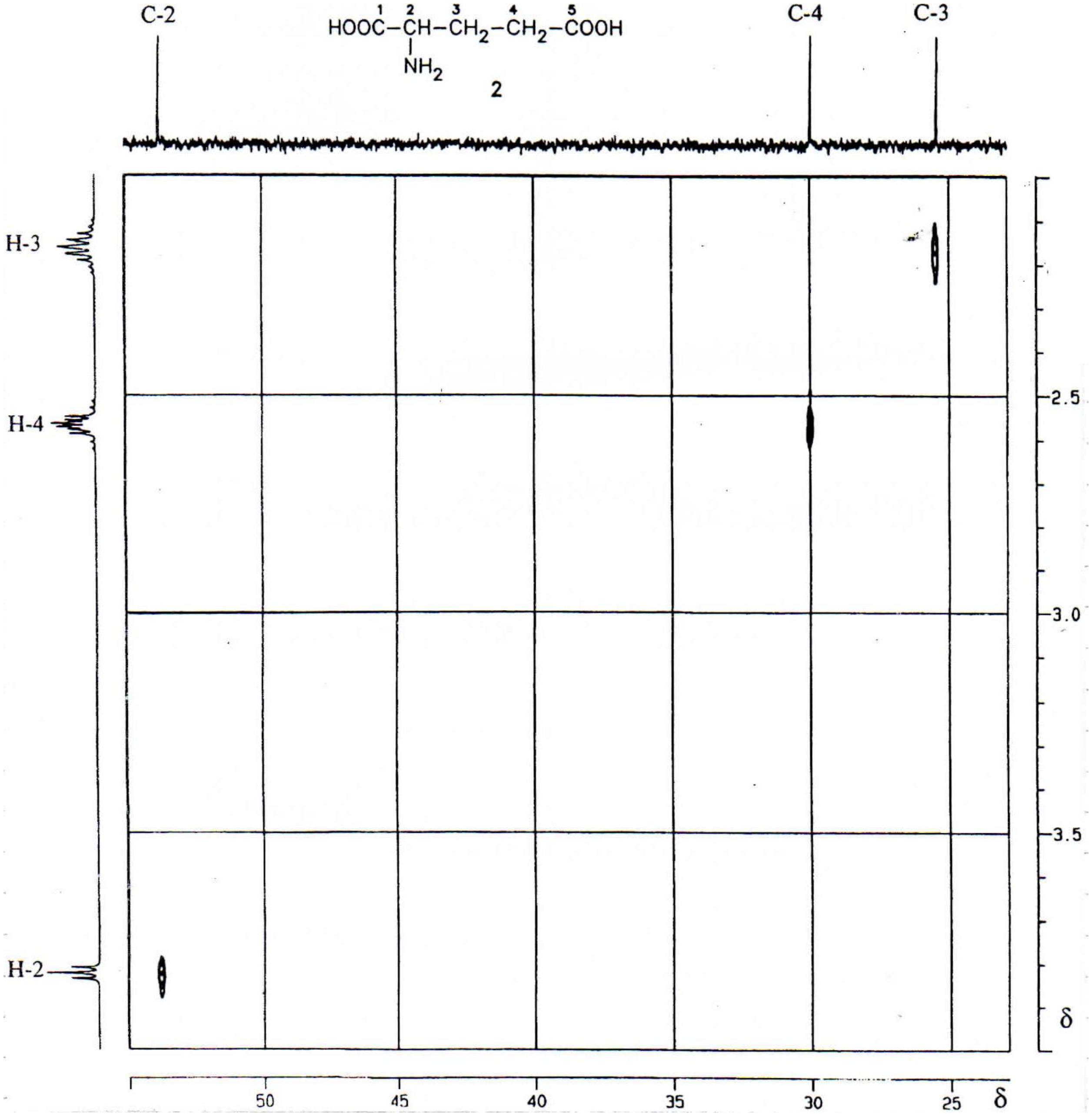
- Nel secondo caso il nucleo osservato (F2) è il $^{1}$H (molto sensibile) = HSQC, HMQC TECNICHE INVERSE

# HETCOR: Heteronuclear Correlation



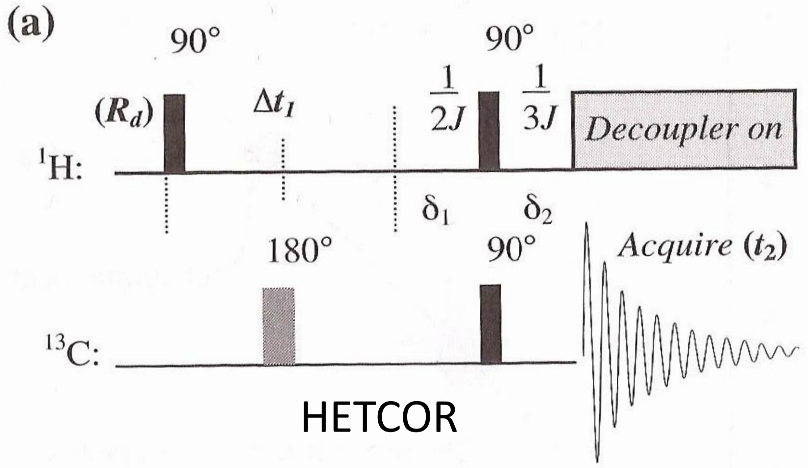
$\Delta_1 = \Delta_2 = 1/2J$

Trasferimento di polarizzazione

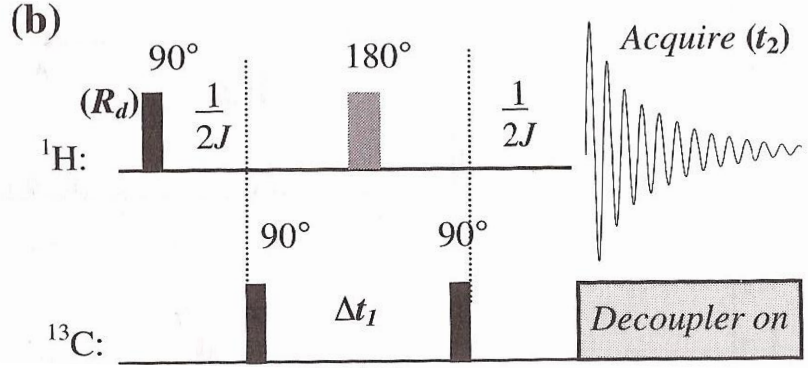

C-2
1 2 3 4 5
HOOC–CH–CH2–CH2–COOH
NH2
2
C-4
C-3
H-3
H-4
H-2
2.5
3.0
3.5
δ
50
45
40
35
30
25
δ

# HMQC

## **H**eteronuclear **M**ultiple **Q**uantum **Co**rrelation



HETCOR



HMQC

Stesse informazioni di HETCOR
Minor tempo di acquisizione

Procedura inversa.
Si rileva il nucleo più sensibile

# HSQC

## Heteronuclear Single Quantum Correlation

Evolve solo la magnetizzazione del $^{13}$C

Stesse informazioni
Minor tempo di acquisizione

INEPT

$^{1}$H

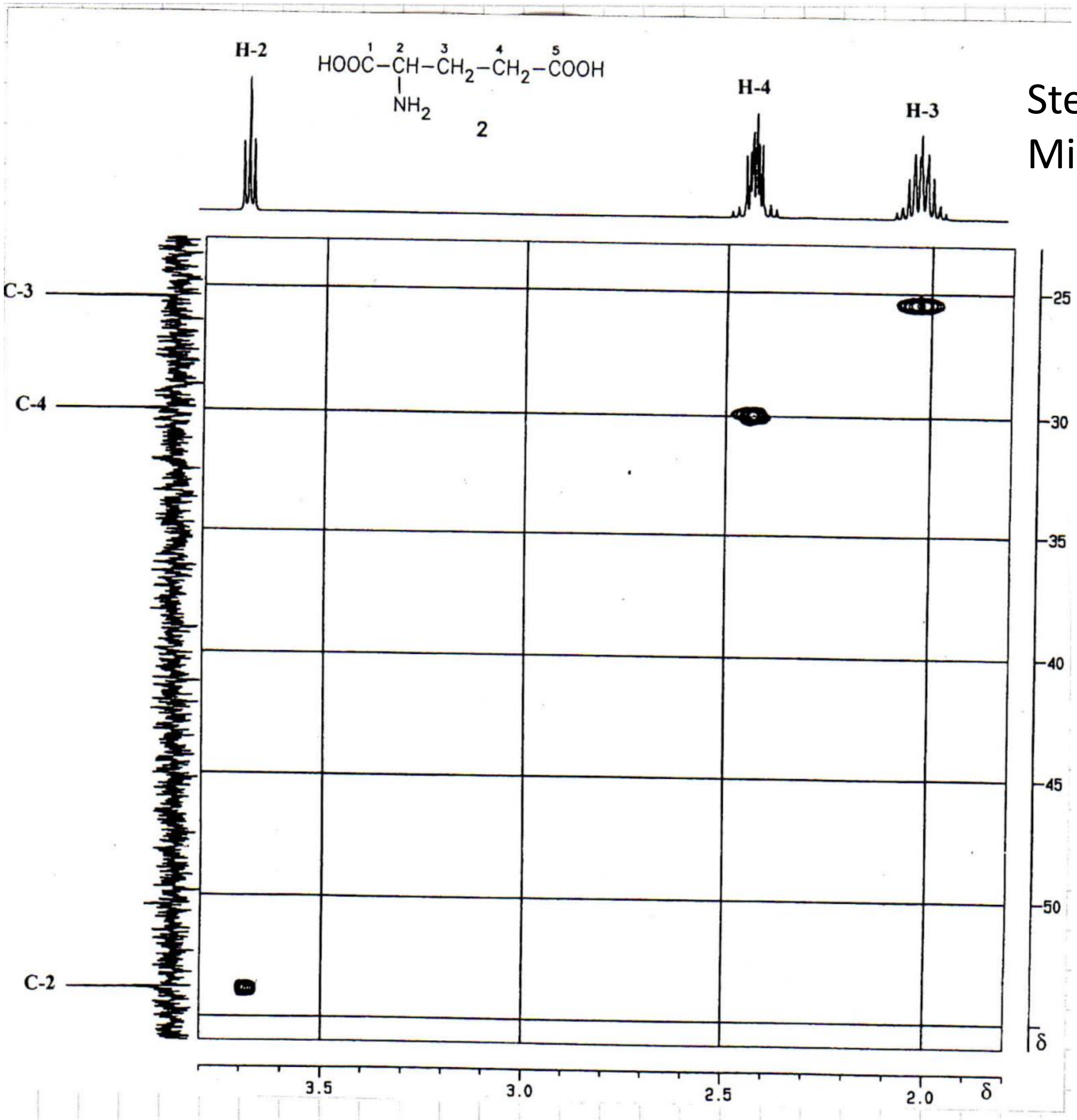
90°x – $\tau$-180°x – 90°y – $t_1$/2 -180°y – $t_1$/2 – 90°x –$\tau$ – 180°x – $\tau$-FID (t2)

$^{13}$C

$\tau$-180°x – $\tau$–90°x' – $t_1$ – 90°x –$\tau$ – 180°x – $\tau$-BB

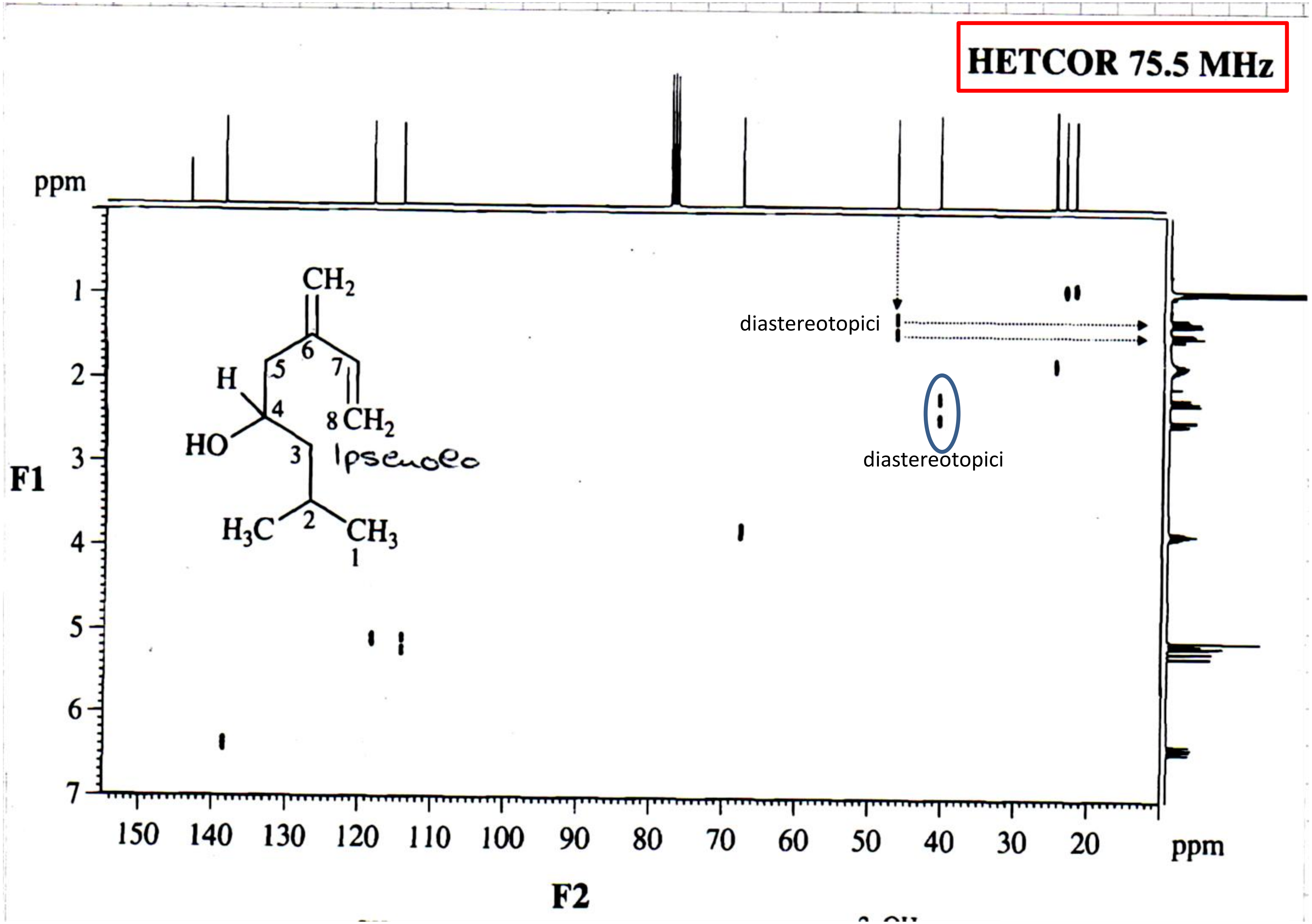
# HSQC

## **Heteronuclear Single Quantum Correlation**



Stesse informazioni
Minor tempo di acquisizione

# HETCOR

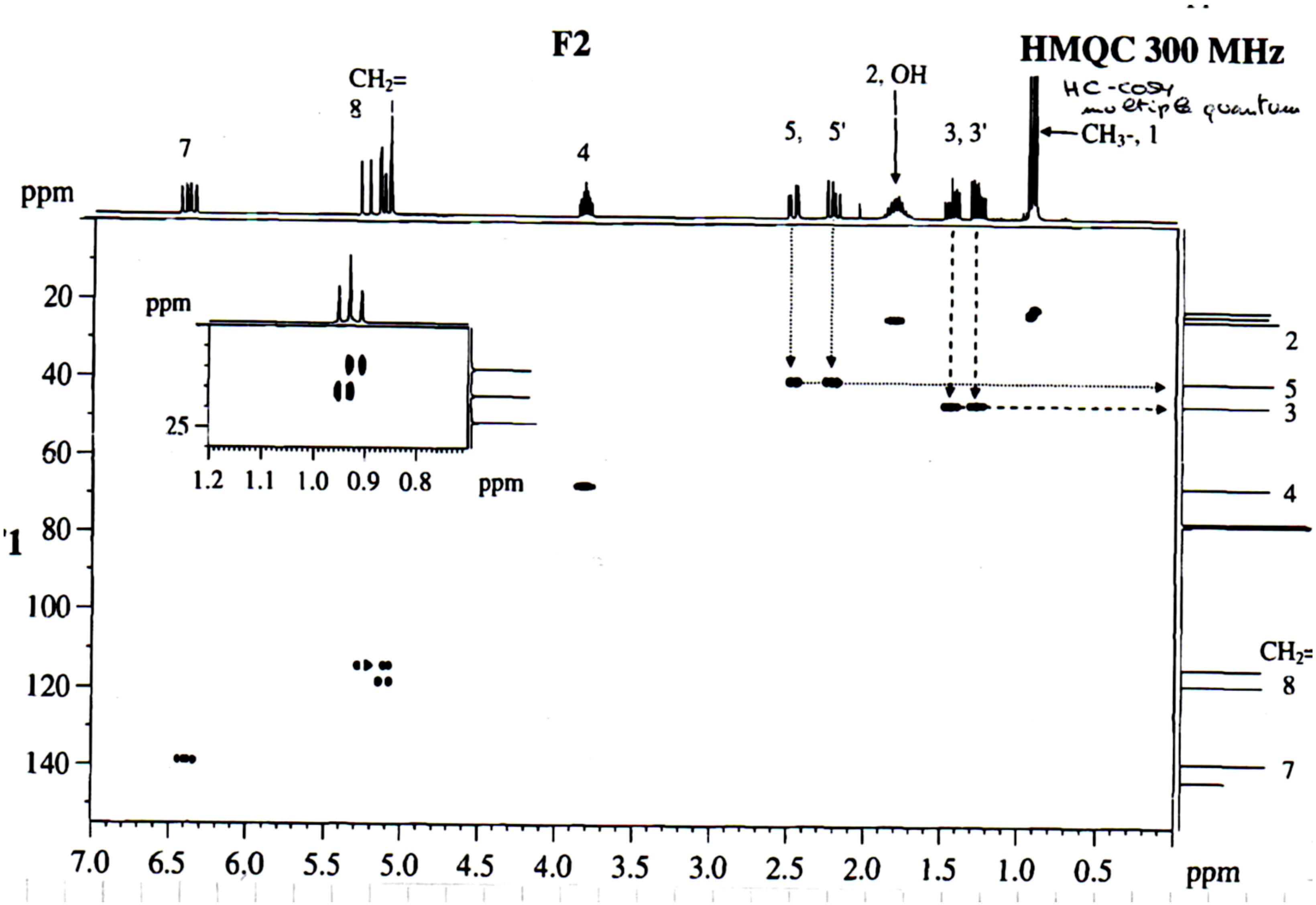


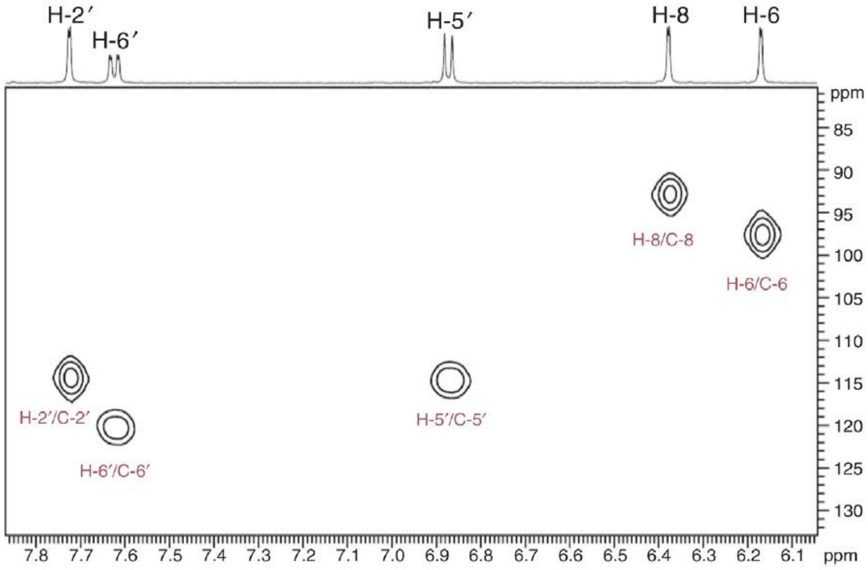
HETCOR 75.5 MHz

diastereotopici

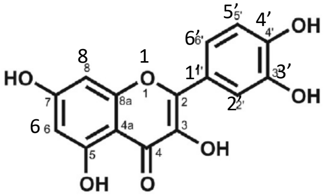
diastereotopici

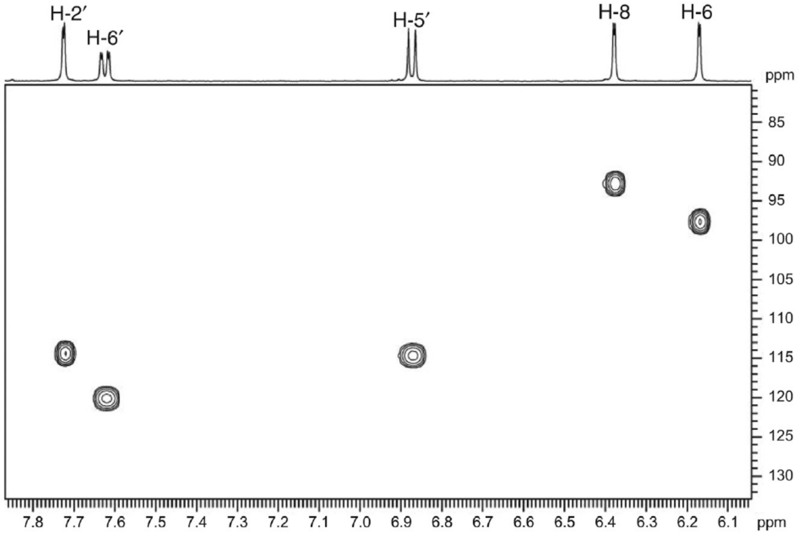
# HMQC


F2
HMQC 300 MHz
HC-COSY
multiple quantum
CH$_2$=
8
7
4
5, 5'
2, OH
3, 3'
←CH$_3$-, 1
ppm
20
40
60
80
100
120
140
F1
ppm
25
1.2 1.1 1.0 0.9 0.8
ppm
2
5
3
4
CH$_2$=
8
7
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
ppm


H-2′
H-6′
H-5′
H-8
H-6
ppm
85
90
95
100
105
110
115
120
125
130
H-8/C-8
H-6/C-6
H-2′/C-2′
H-6′/C-6′
H-5′/C-5′
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4
6.3
6.2
6.1
ppm

HMQC

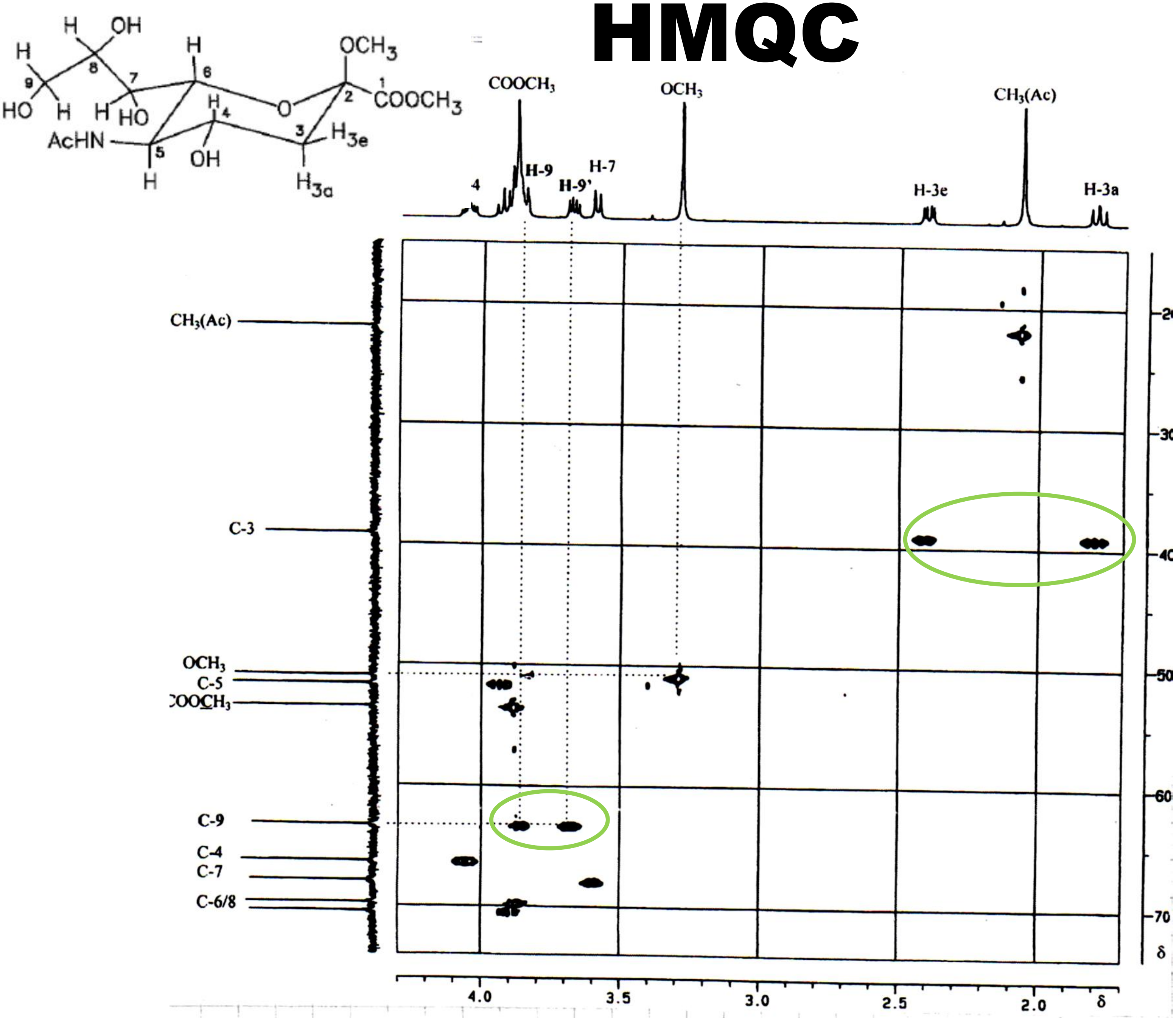

HO
OH
OH
OH
OH
O
O
1
2
3
4
4a
5
6
7
8
8a
1′
2′
3′
4′
5′
6′


H-2′
H-6′
H-5′
H-8
H-6
ppm
85
90
95
100
105
110
115
120
125
130
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4
6.3
6.2
6.1
ppm

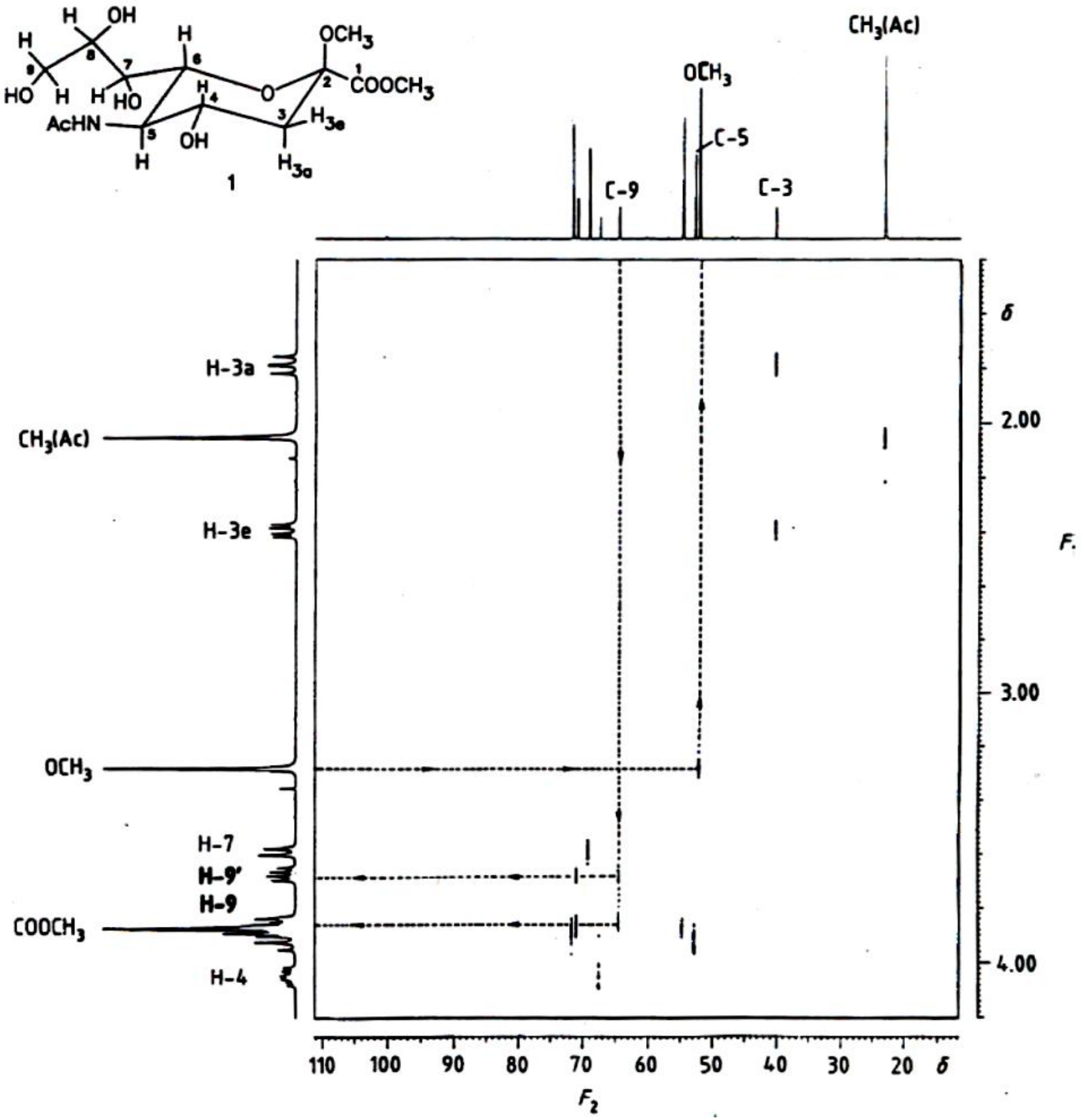
HSQC

# HMQC

HSQC

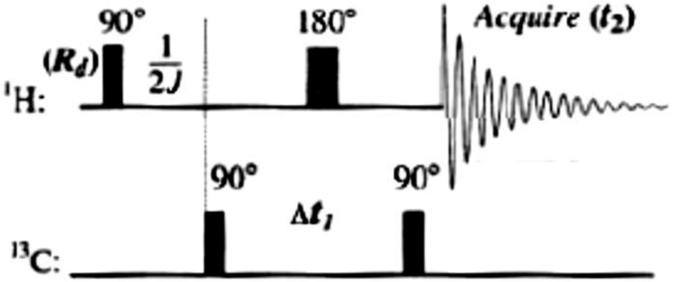

H
OH
H
8
9
7
6
H
OCH3
1
2
COOCH3
HO
H
H
HO
H
4
O
3
H3e
AcHN
5
OH
H
H3a
COOCH3
OCH3
CH3(Ac)
4
H-9
H-9'
H-7
H-3e
H-3a
CH3(Ac)
C-3
OCH3
C-5
COOCH3
C-9
C-4
C-7
C-6/8
20
30
40
50
60
70
δ
4.0
3.5
3.0
2.5
2.0
δ

# HETCOR



HETCOR

# HMBC
# Heteronuclear Multiple Bond Coherence

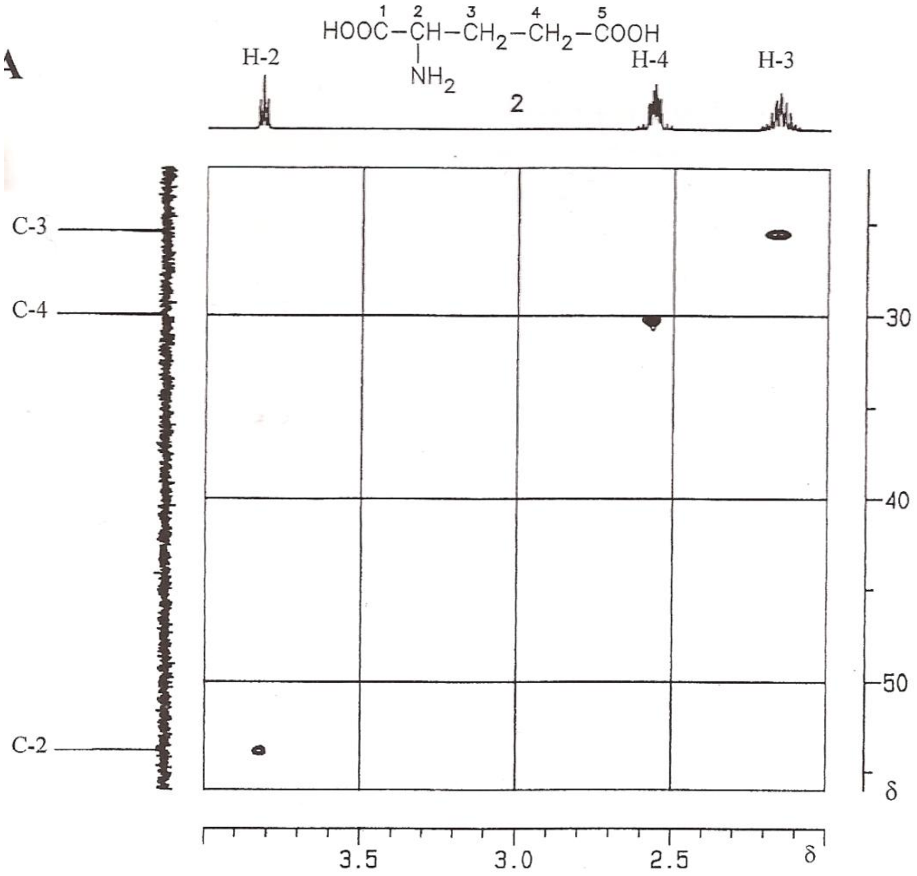


FILTRA GLI ACCOPPIAMENTI $^1J_{CH}$

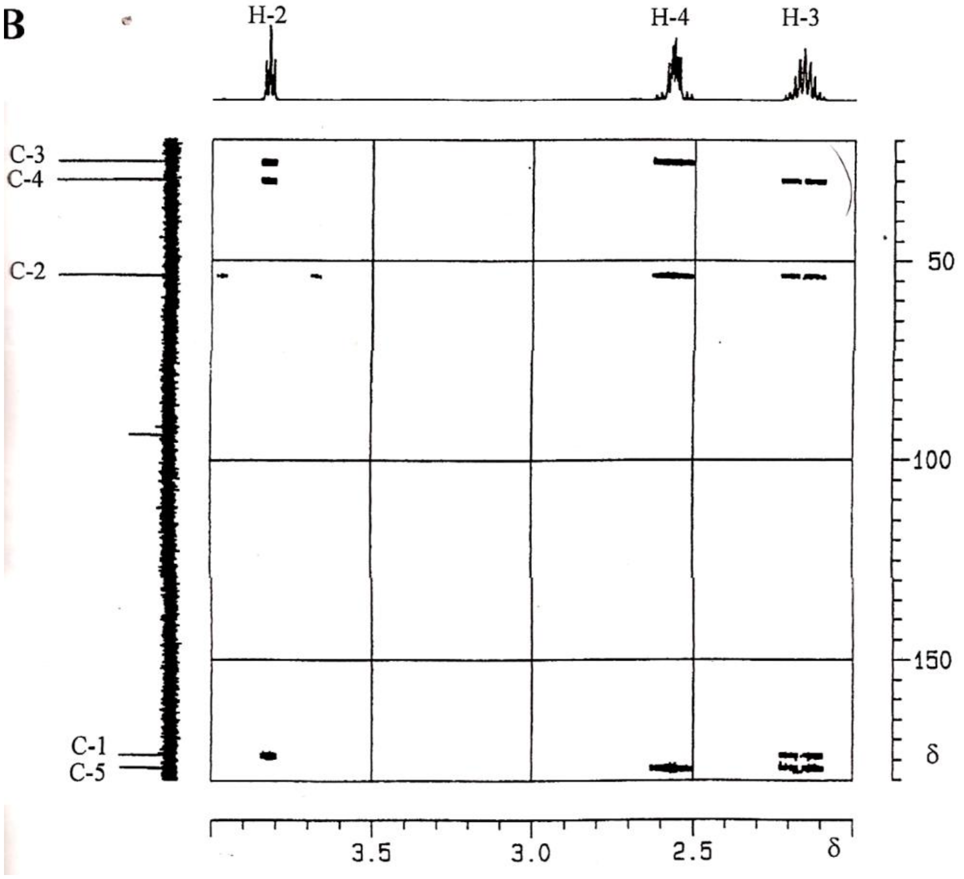
SI VEDONO GLI ACCOPPIAMENTI $^2J_{CH}$ e $^3J_{CH}$

# HMBC

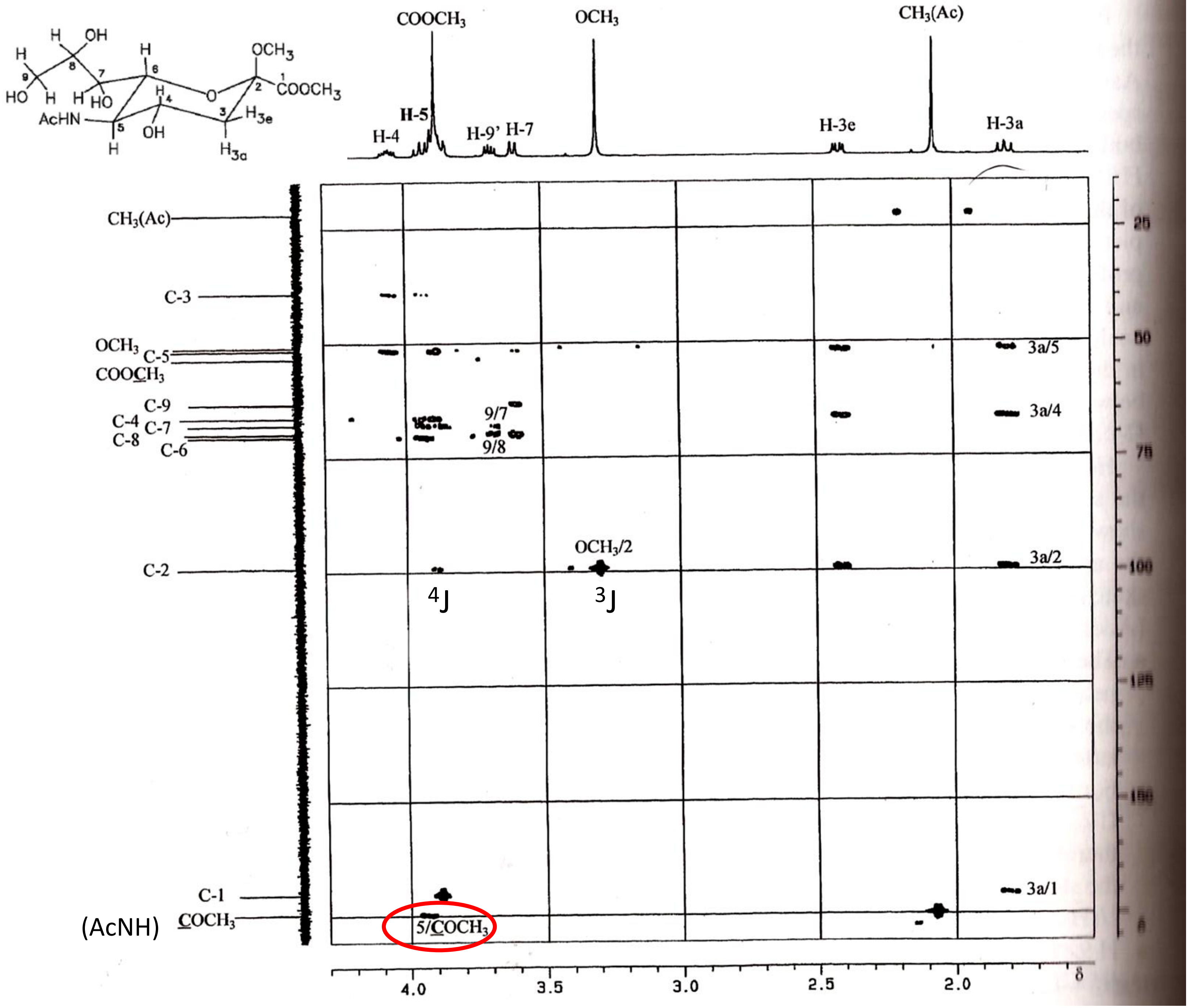
# Heteronuclear Multiple Bond Coherence



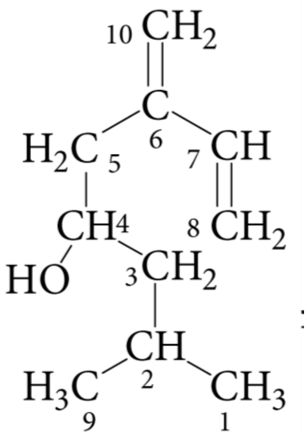
HSQC



HMBC

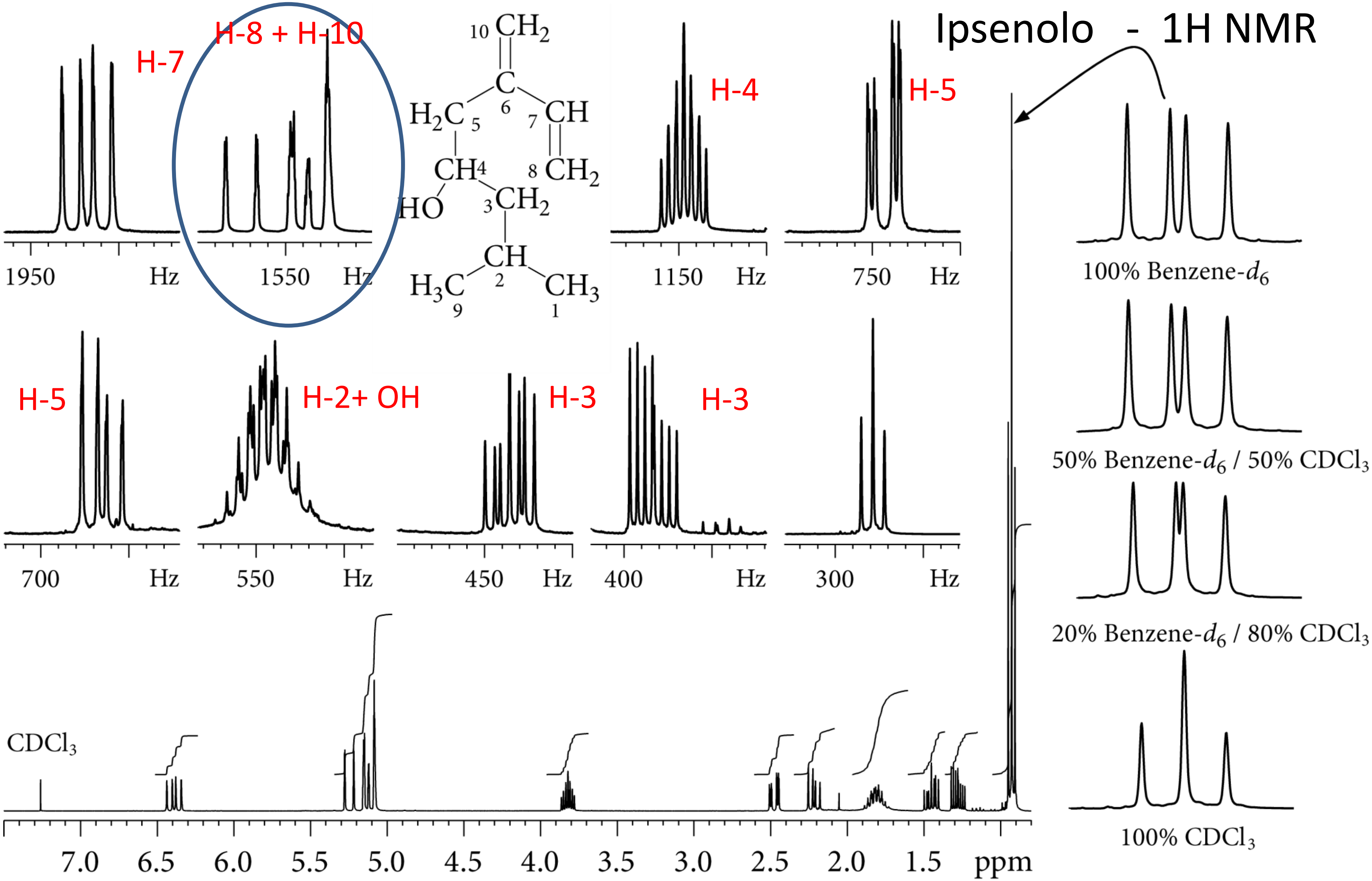

OCH3
COOCH3
AcHN
H3e
H3a
COOCH3
OCH3
CH3(Ac)
H-4
H-5
H-9'
H-7
H-3e
H-3a
CH3(Ac)
C-3
OCH3
C-5
COOCH3
C-9
C-4
C-7
C-8
C-6
C-2
C-1
(AcNH)
COCH3
3a/5
3a/4
9/7
9/8
OCH3/2
3a/2
4J
3J
3a/1
5/COCH3
4.0
3.5
3.0
2.5
2.0
δ
25
50
75
100
125
150

Identificare i segnali dei gruppi =$CH_2$ nelle posizioni 8 e 10.



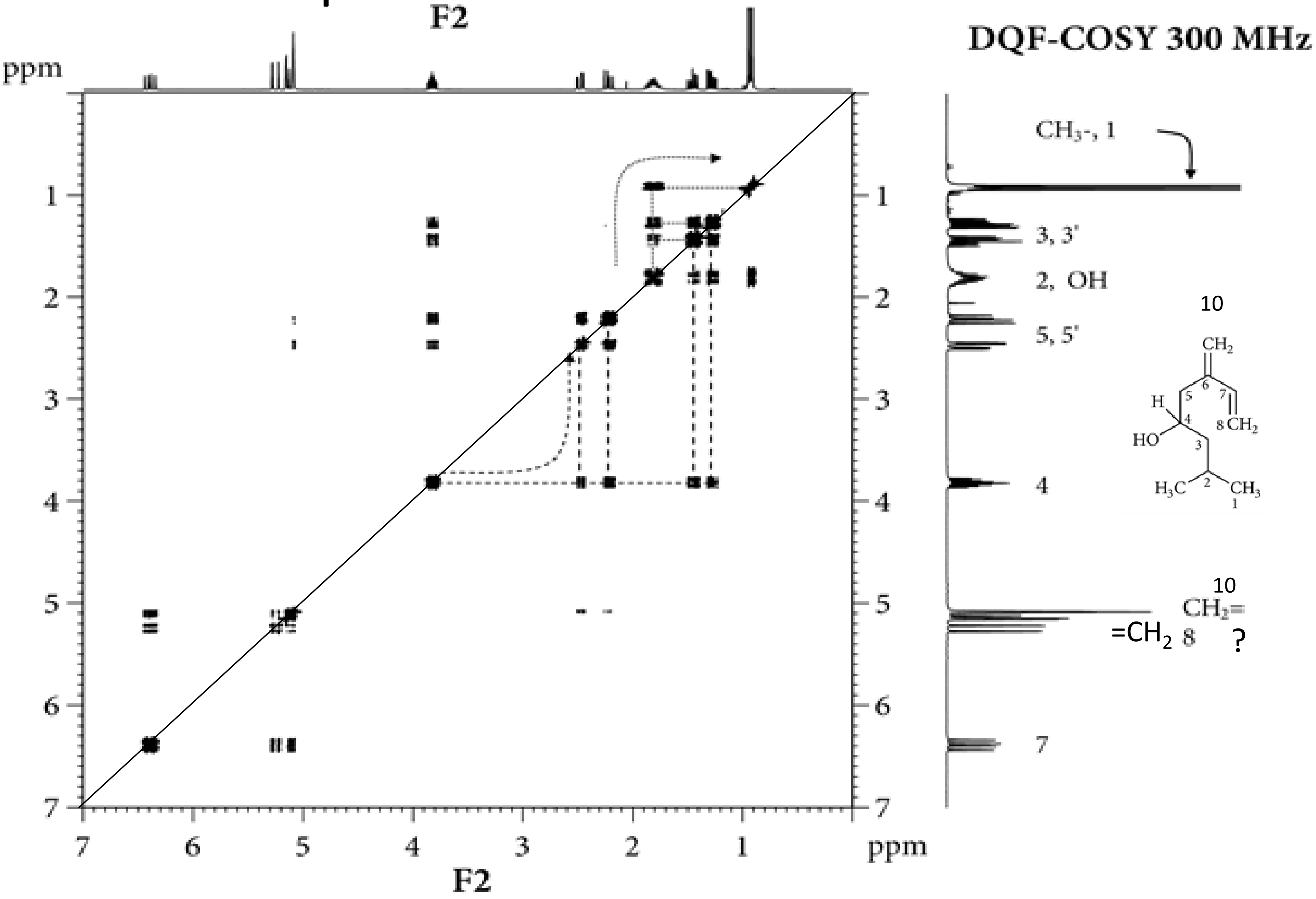
Ipsenolo

# Ipsenolo - 1H NMR

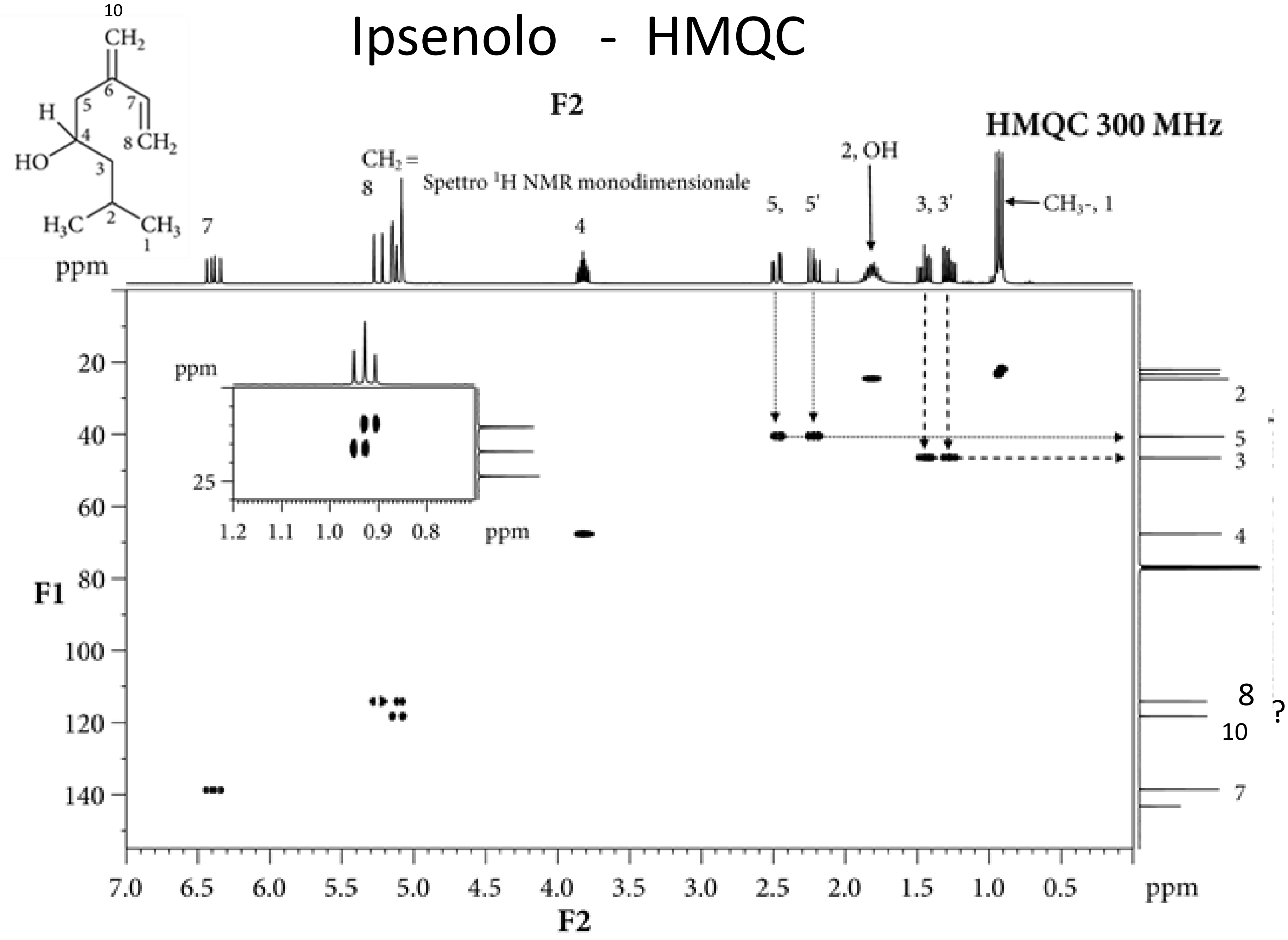


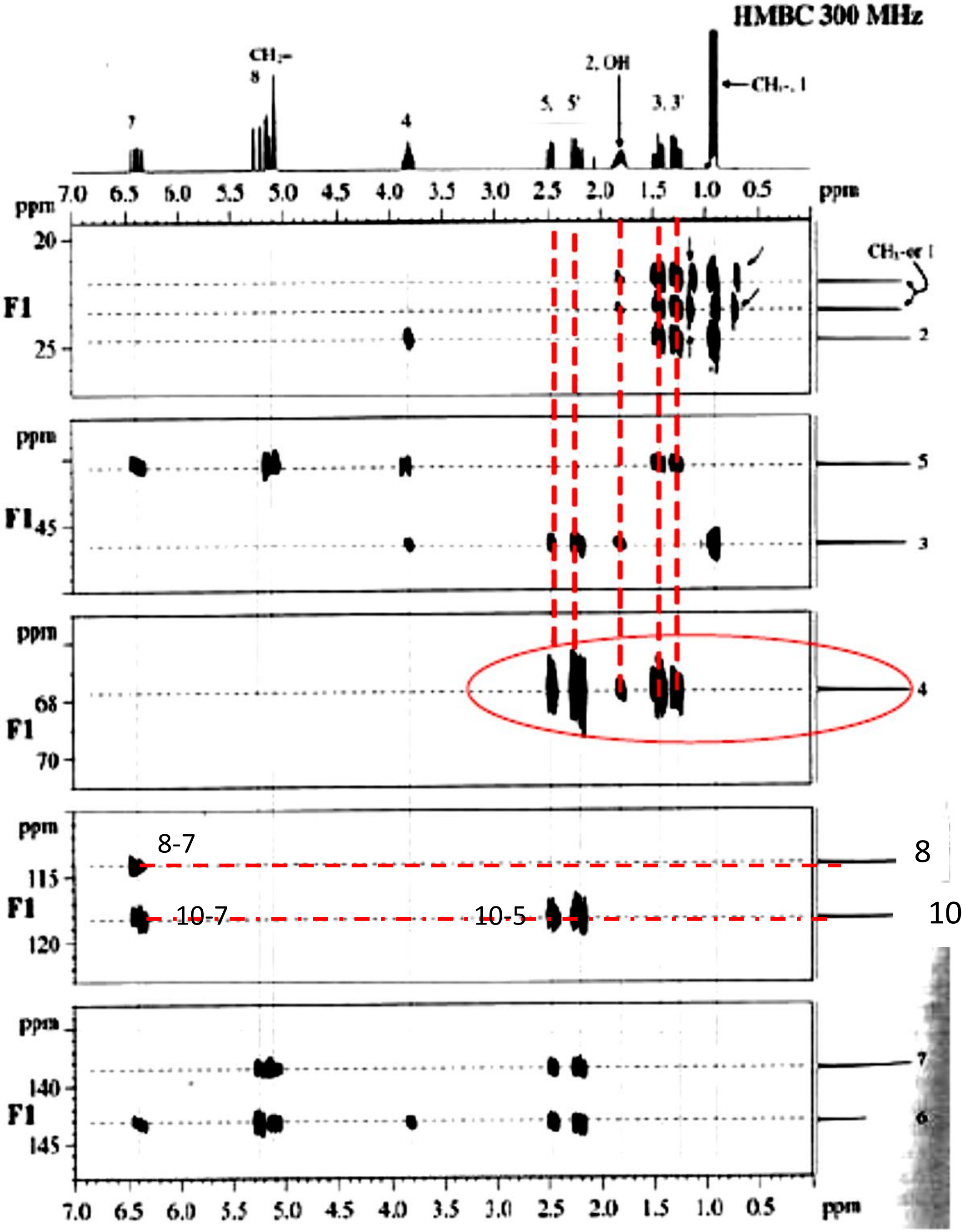
Spettro protonico NMR di 2-metil-6-metilen-7-otten-4-olo (ipsenolo) in $CDCl_3$ a 300 MHz ed effetto della titolazione con benzene-$d_6$.

# Ipsenolo - COSY

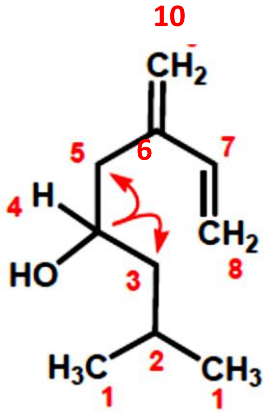


# Ipsenolo - HMQC

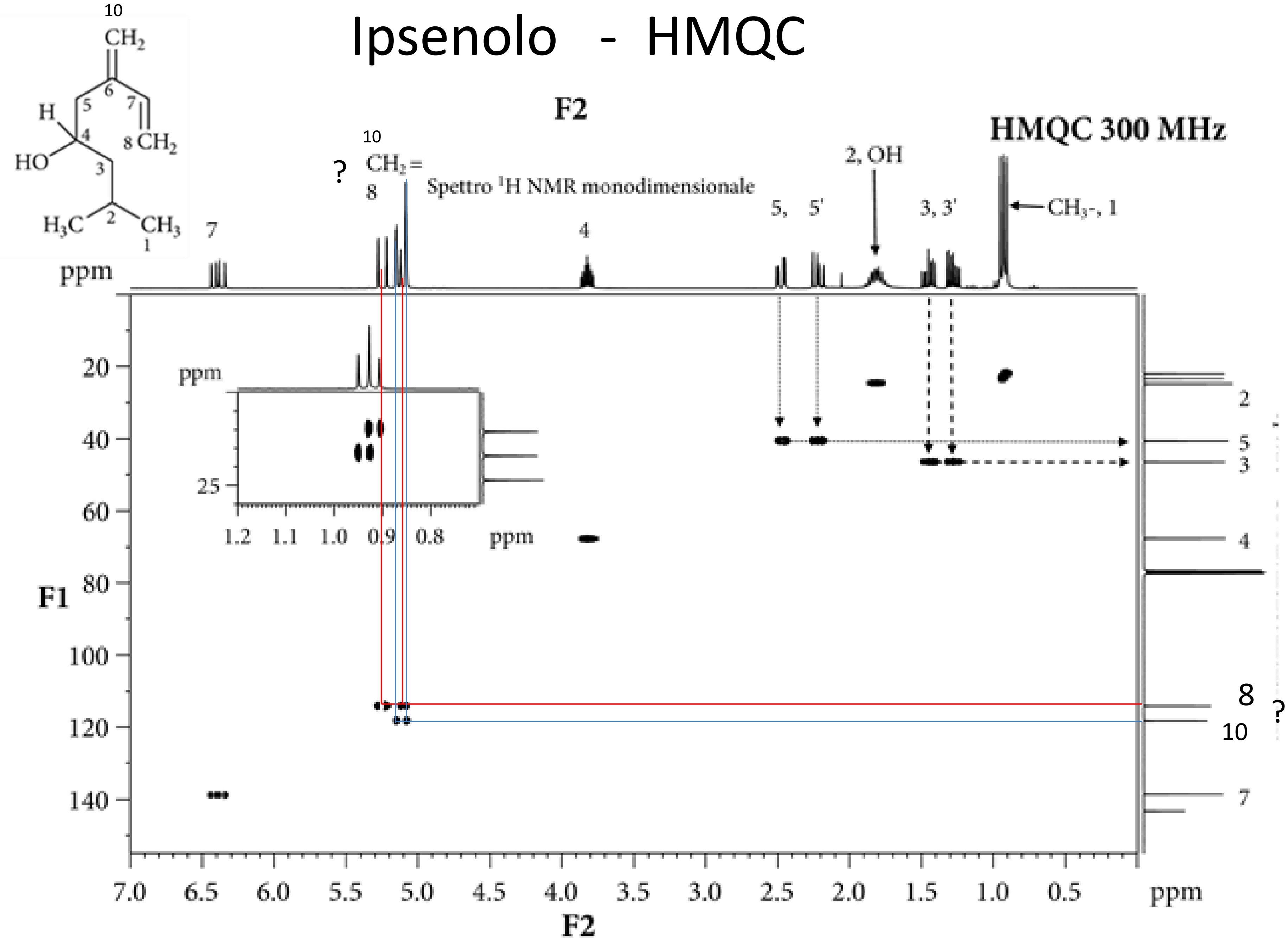




Non si osservano costanti dirette



# Ipsenolo - HMQC



# J RESOLVED NMR 2D

Gli esperimenti J resolved separano l'informazione del chemical shift ($\nu_1$) da quella della *J* ($\nu_2$) lungo le due dimensioni dello spettro consentendo l'assegnazione esatta di chemical shift e J di multipletti sovrapposti nello spettro 1D.

Versioni omo- ed eteronucleari

## 1. HETERONUCLEAR (C-H) J-RESOLVED 2D

Derivano dalla variazione periodica del segnale del $^{13}C$ durante $t_1$ ad opera della $J_{CH}$ (frequenza di modulazione)

Si usa una sequenza uguale alla 1D J-MODULATED SPIN ECHO, con $t_1$ variabile in maniera incrementale. Il decoupler è acceso ad intermittenza, in particolare viene spento durante la prima metà del $t_1$.