

QFL-1345

RMN de  $^{13}\text{C}$

19 de junho de 2023

## Características de alguns elementos ativos em RMN (e as dificuldades em se obter os espectros de RMN de $^{13}\text{C}$ )

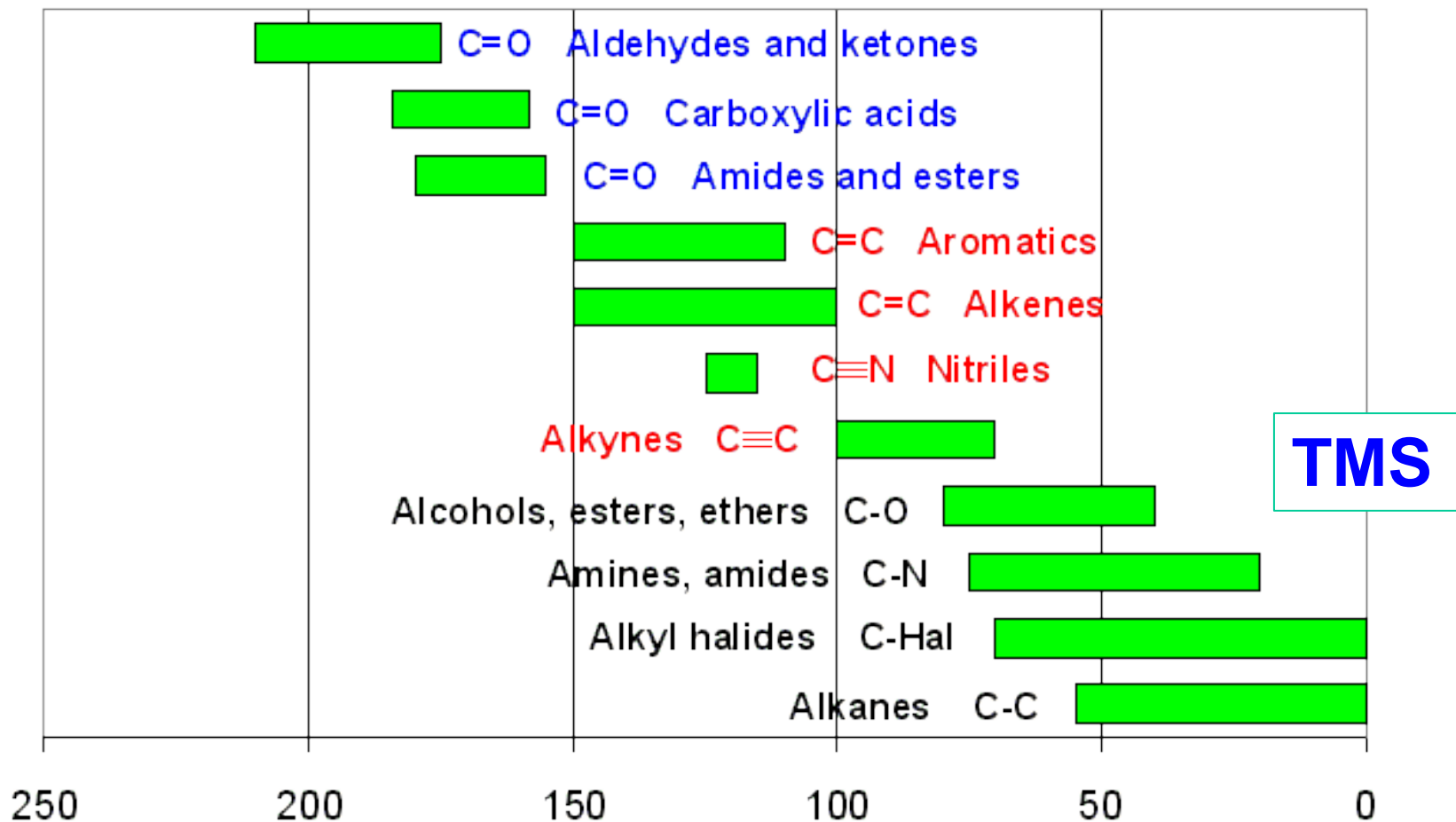
Isotope	$\gamma$ (relative)	resonance frequency at 11.7 T	natural abundance	relative sensitivity*
$^1\text{H}$	100	500 MHz	99.98 %	1
$^{13}\text{C}$	25	125 MHz	1.1 %	$10^{-5}$
$^{15}\text{N}$	-10	50 MHz	0.37 %	$10^{-7}$
$^{19}\text{F}$	94	455 MHz	100 %	0.8
$^{29}\text{Si}$	-20	99 MHz	4.7 %	$10^{-3}$
$^{31}\text{P}$	40	203 MHz	100 %	0.07

- also taking into account typical linewidths and relaxation rates

# Principais informações obtidas de um espectro de RMN de $^{13}\text{C}$ NMR

- 1) Posição de absorção (deslocamento químico em  $\delta$  - ppm);
- 2) Tipos de carbonos ( $\text{CH}_3$ ,  $\text{CH}_2$ ,  $\text{CH}$ ,  $\text{C}$ ):  
(APT, DEPT, Ed-HSQC);
- 3) Proporção de carbonos (quase não se usa);
- 4) Podem ser 2D [COSY (H acoplados);  
HSQC (C-H diretamente ligados);  
HMBC (C-H a 2-4 ligações);  
NOESY e outras]

# Faixas de deslocamentos químicos em RMN de $^{13}\text{C}$



Núcleos desblindados (desprotegidos)

Densidade de elétrons sobre núcleos de  $^{13}\text{C}$

Núcleos blindados (protegidos)

# Tipos de espectros de RMN de $^{13}\text{C}$

(espectros mais comuns)

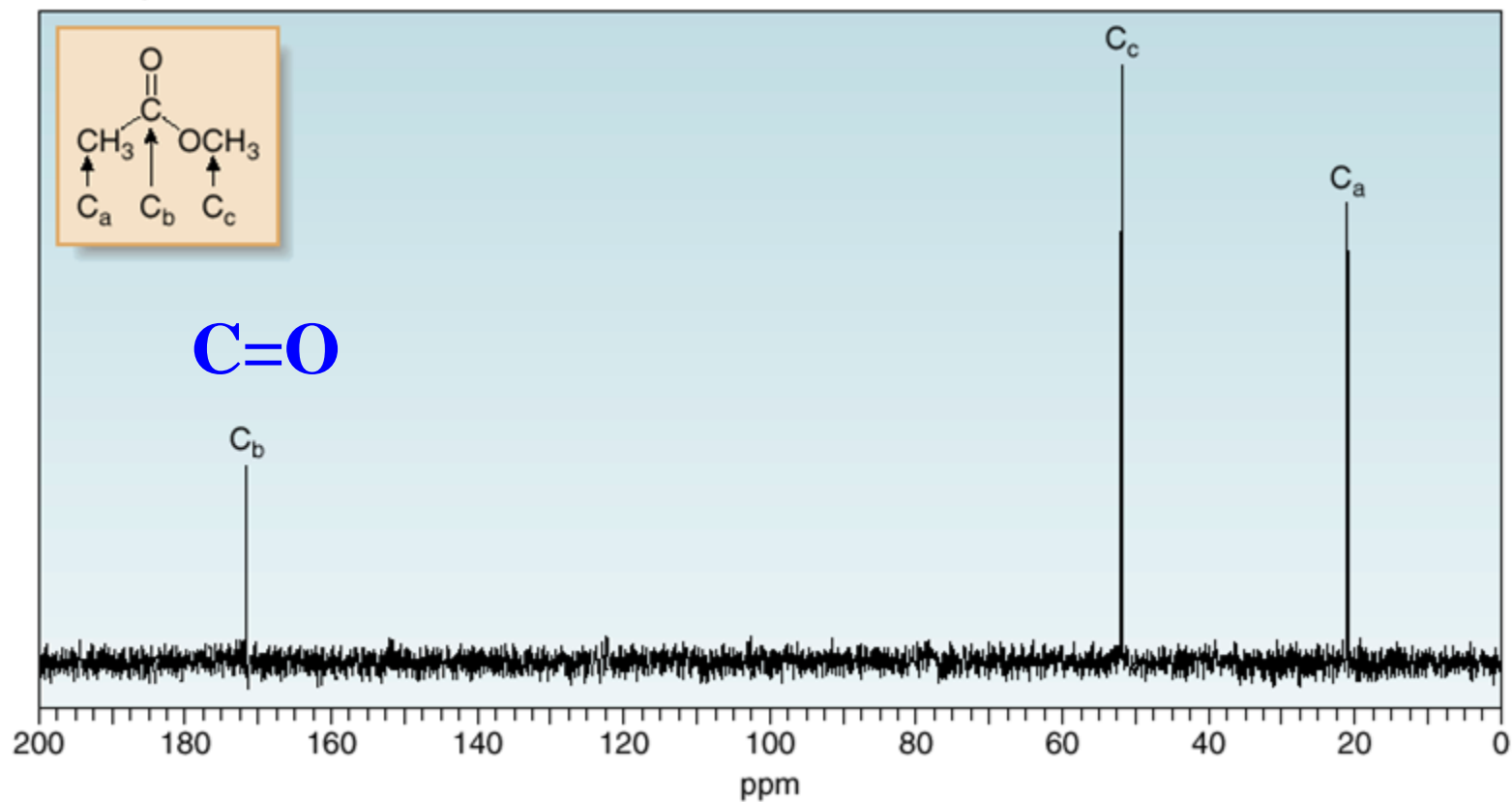
**PND (or BBD): proton noise decoupled  
or broad band decoupled spectra**

Não há acoplamentos entre  $^{13}\text{C}$  e  $^1\text{H}$  e  
cada carbono (C, CH,  $\text{CH}_3$  e  $\text{CH}_3$ )  
se apresenta como um singleto

# Número de sinais em RMN de $^{13}\text{C}$

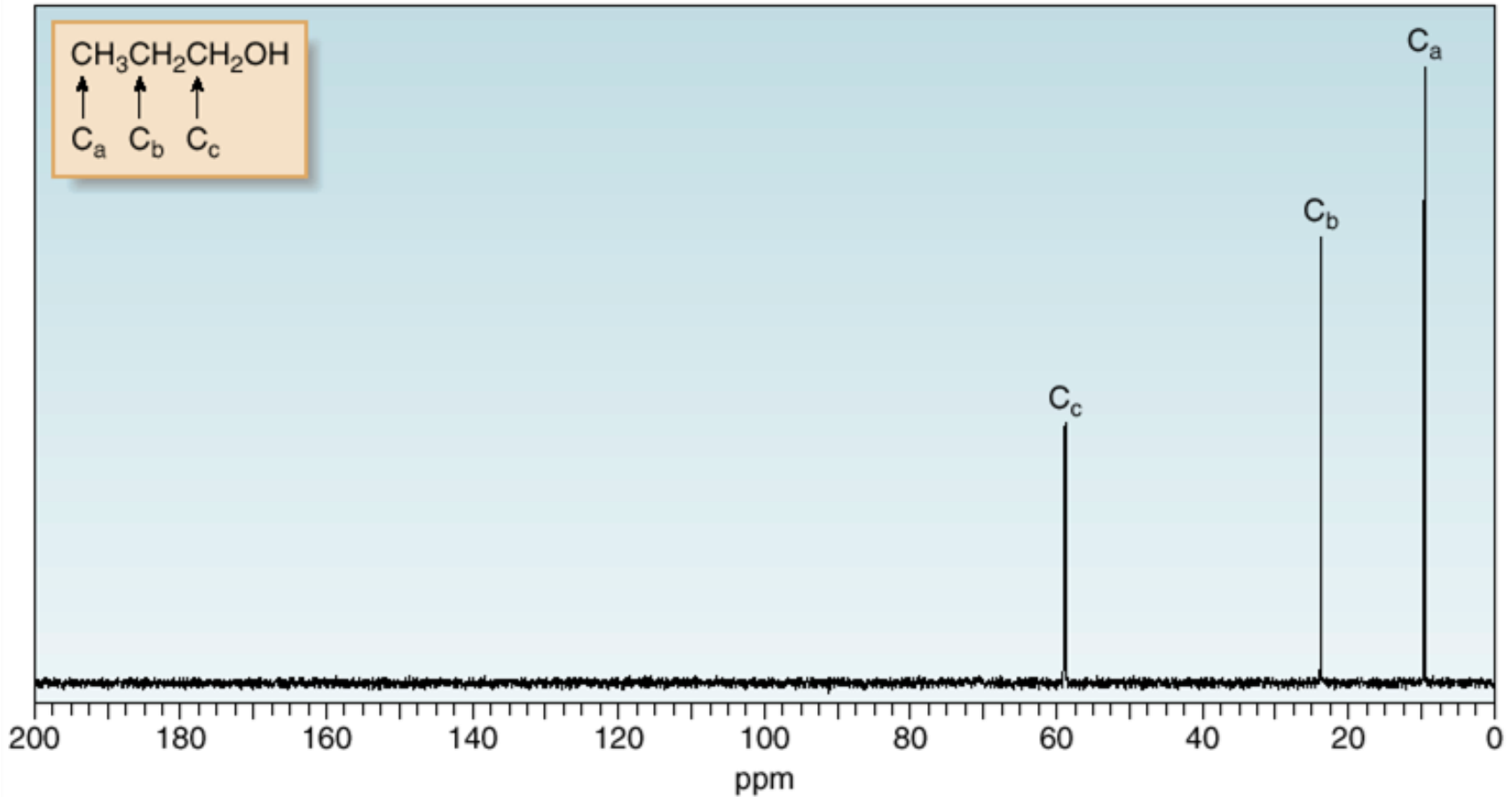
Acetato de metila

$-\text{OCH}_3$      $\text{CH}_3$



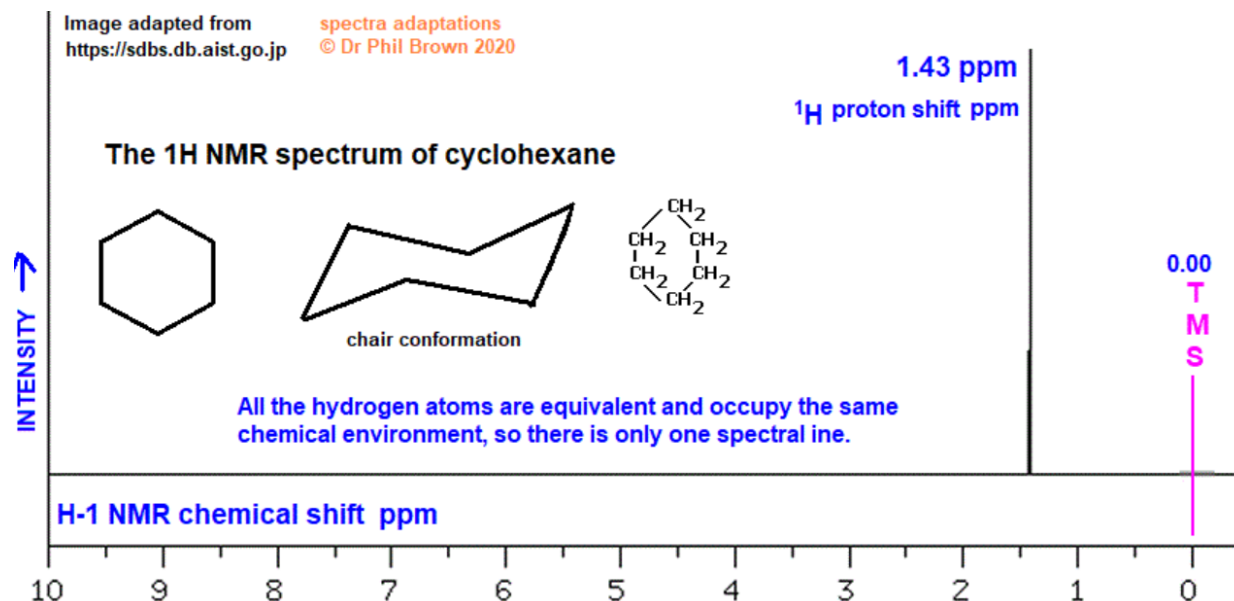
# Espectro de RMN de $^{13}\text{C}$ do propanol

a. 1-Propanol

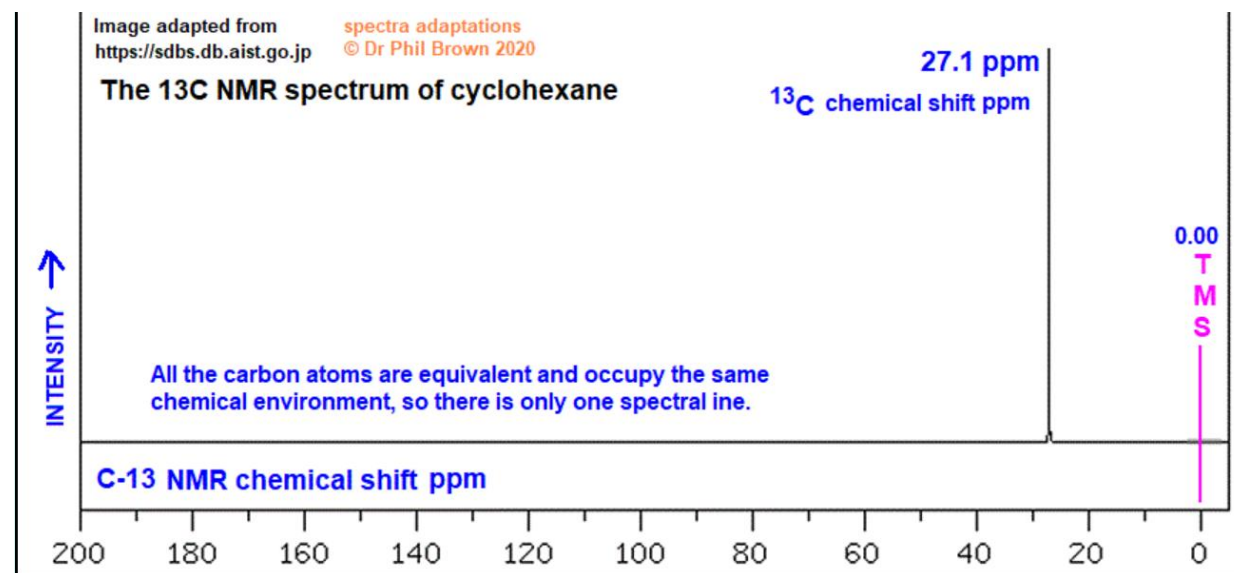


# Espectros de RMN de $^1\text{H}$ e $^{13}\text{C}$ do ciclohexano?

## RMN de $^1\text{H}$

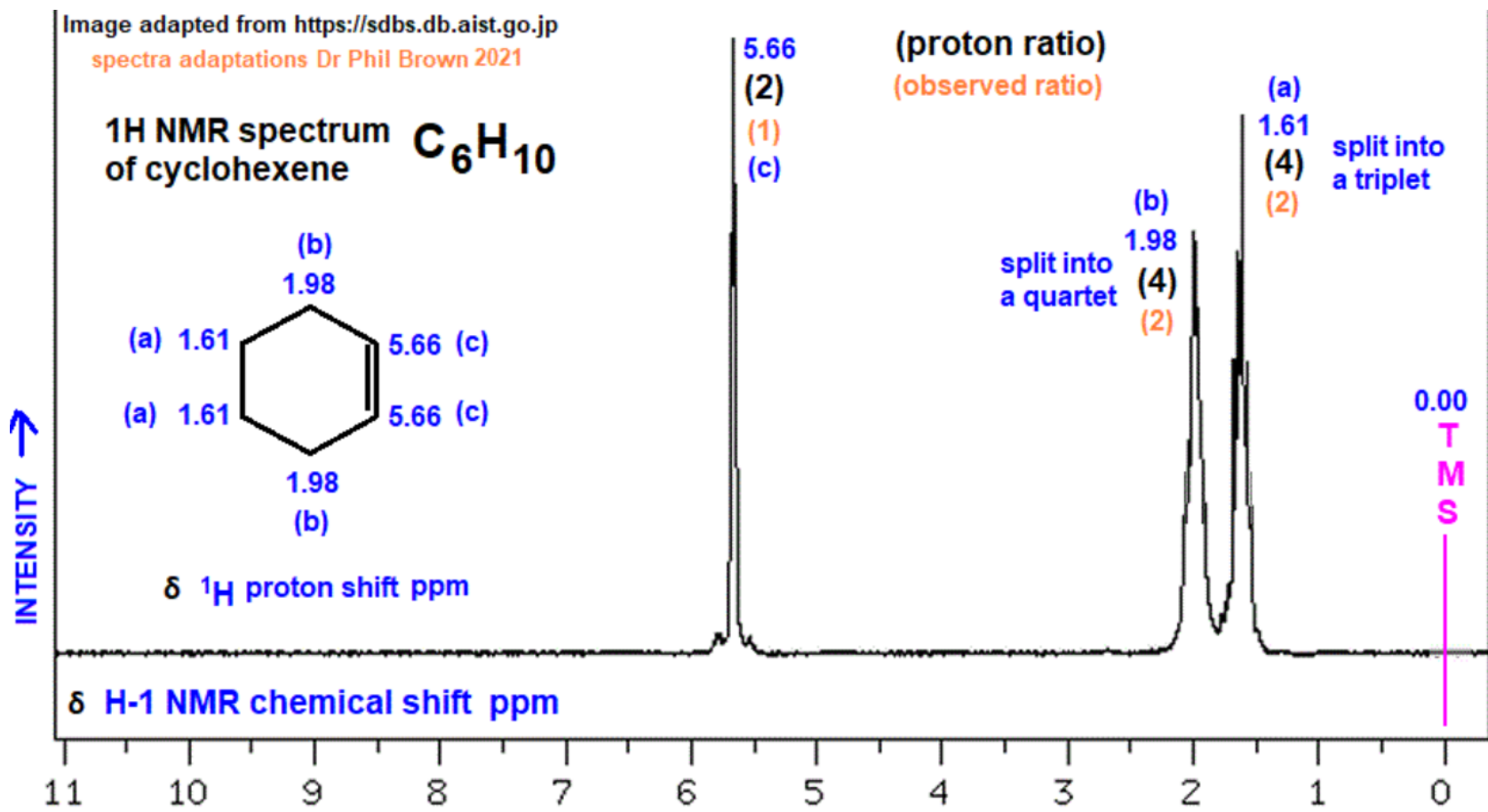


## RMN de $^{13}\text{C}$



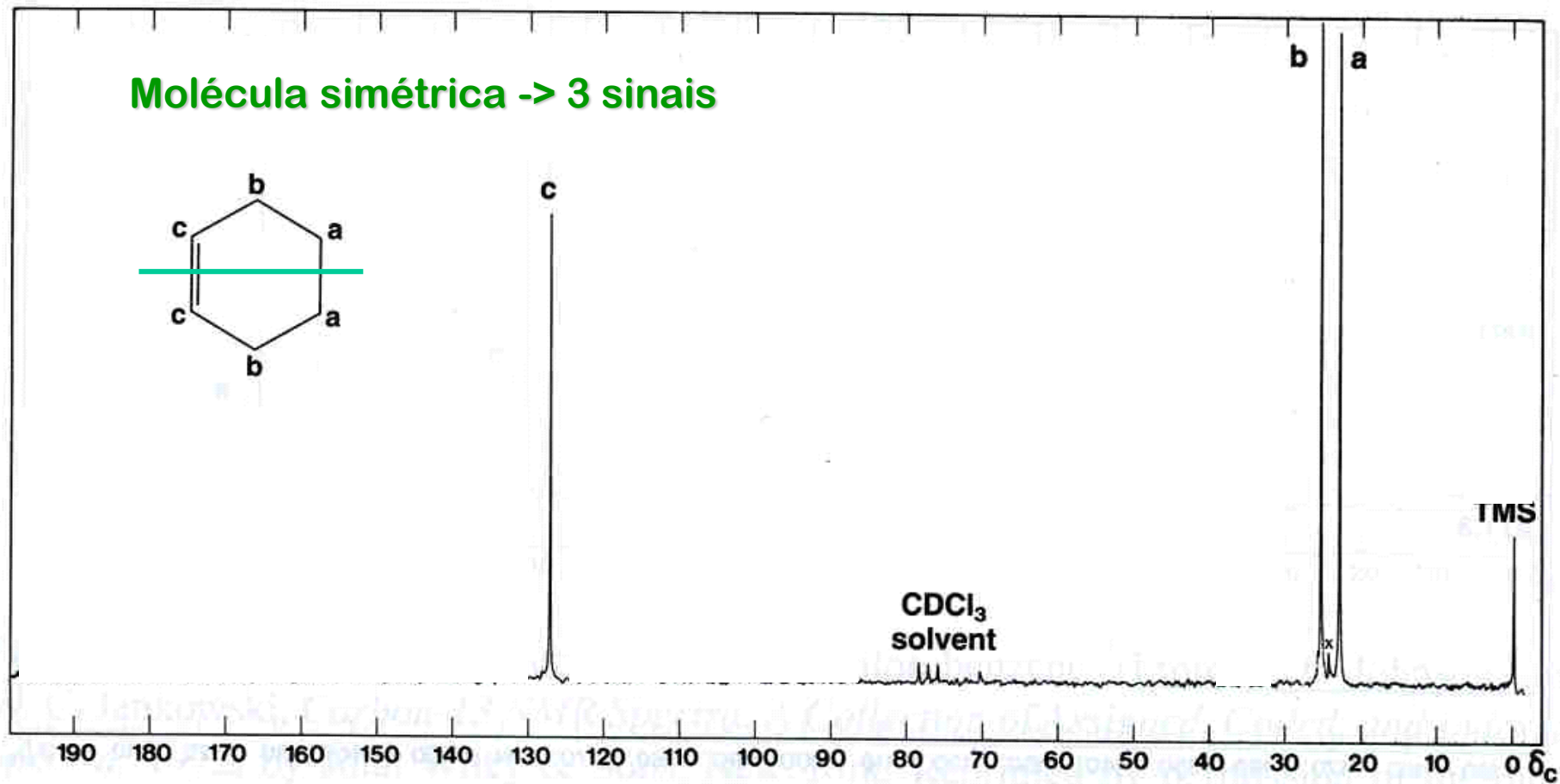
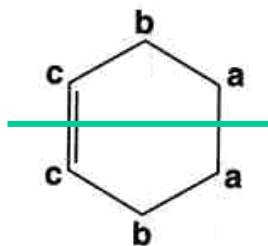


# Espectro de RMN de $^1\text{H}$ do ciclohexeno

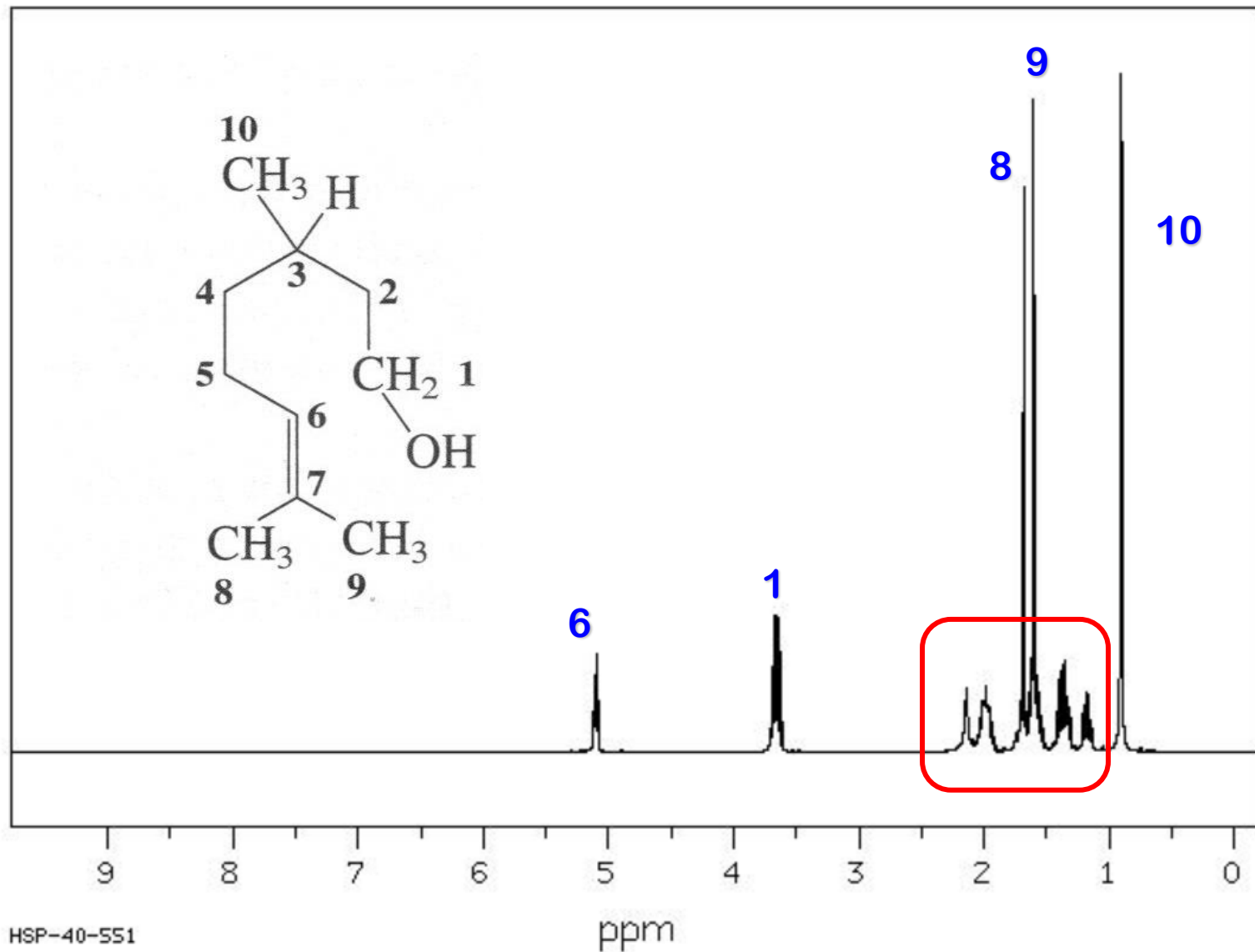


# Espectro de RMN de $^{13}\text{C}$ do ciclohexeno

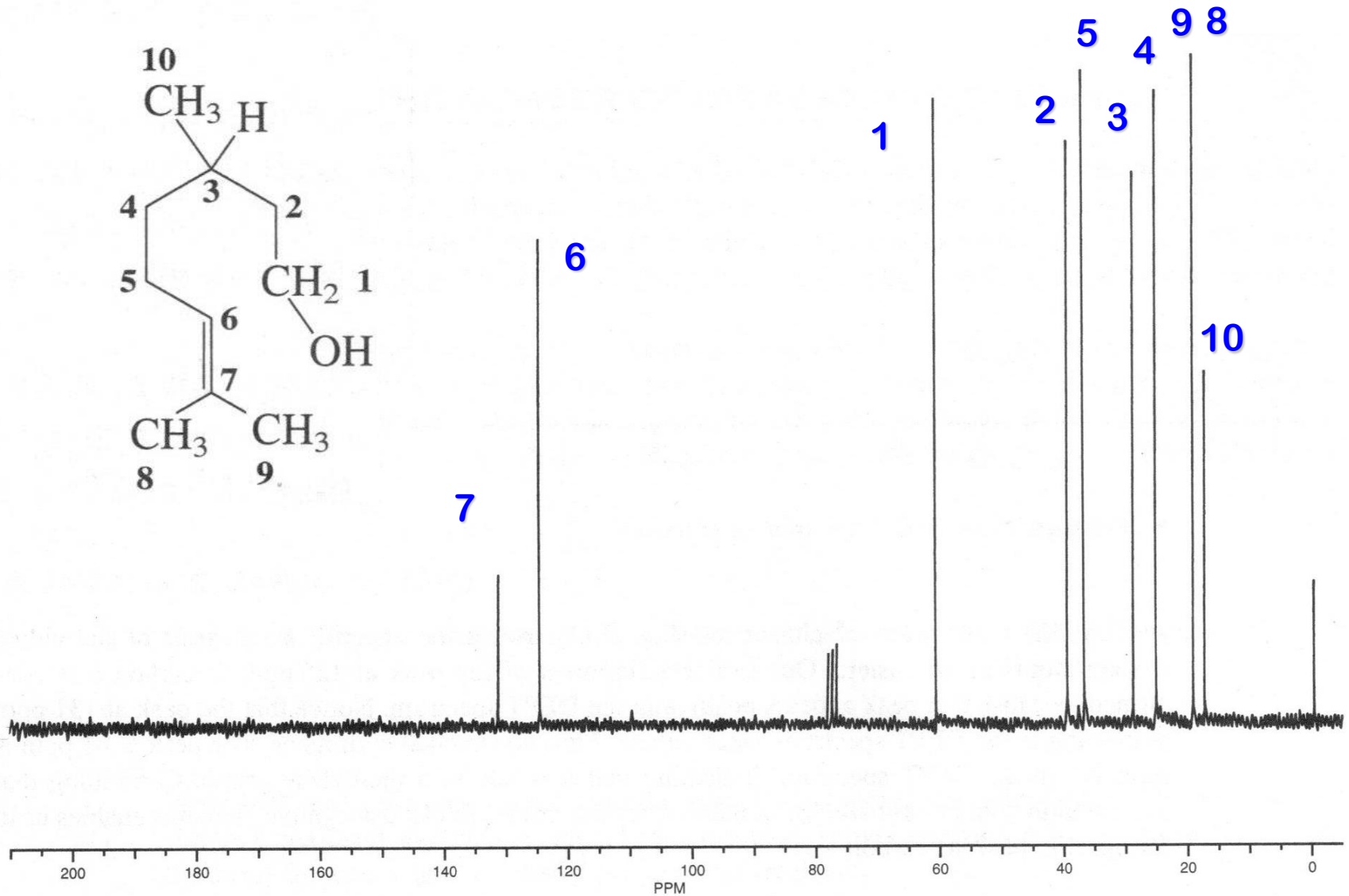
Molécula simétrica -> 3 sinais



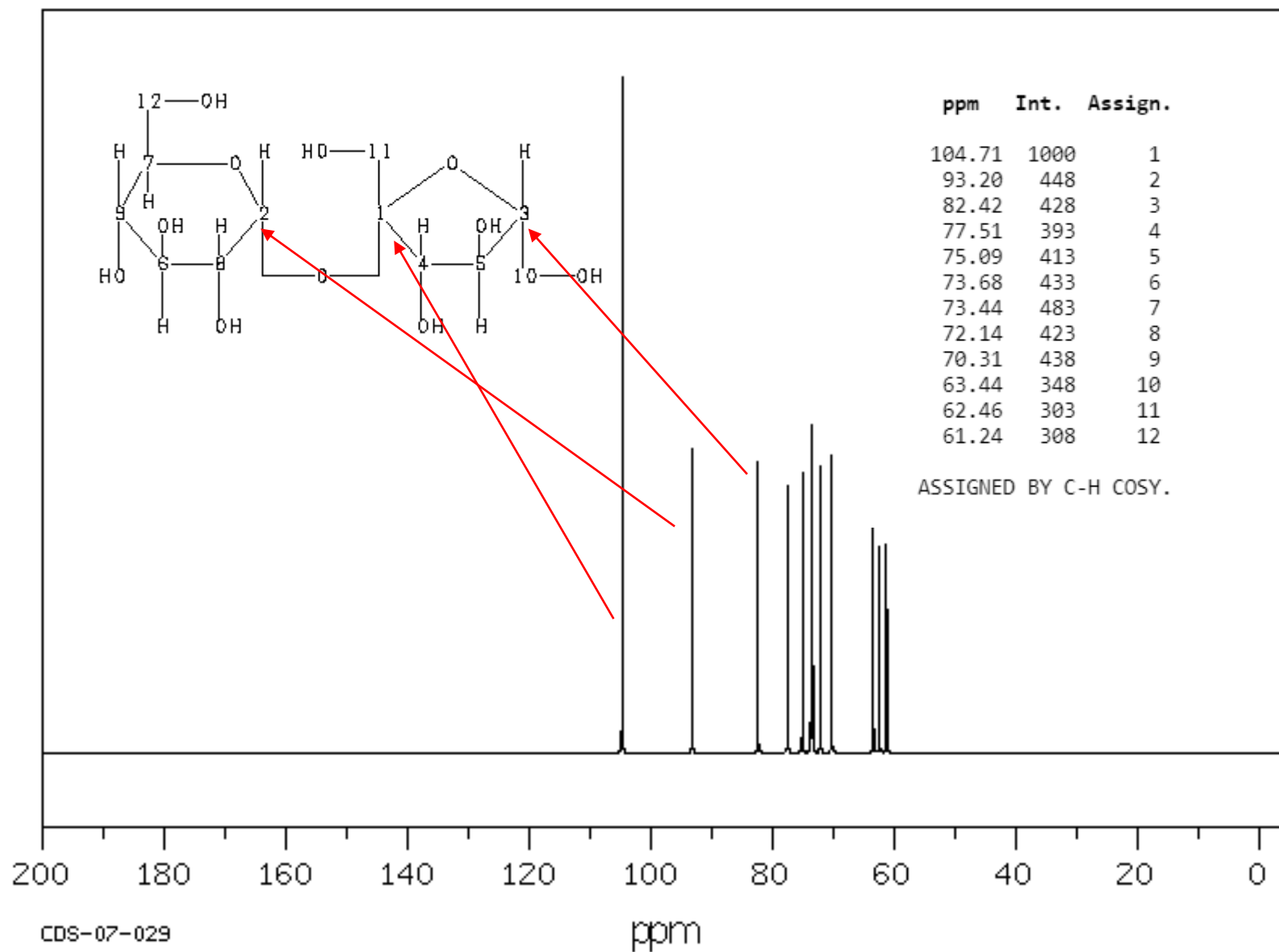
# Espectro de RMN de $^1\text{H}$ do citronelol



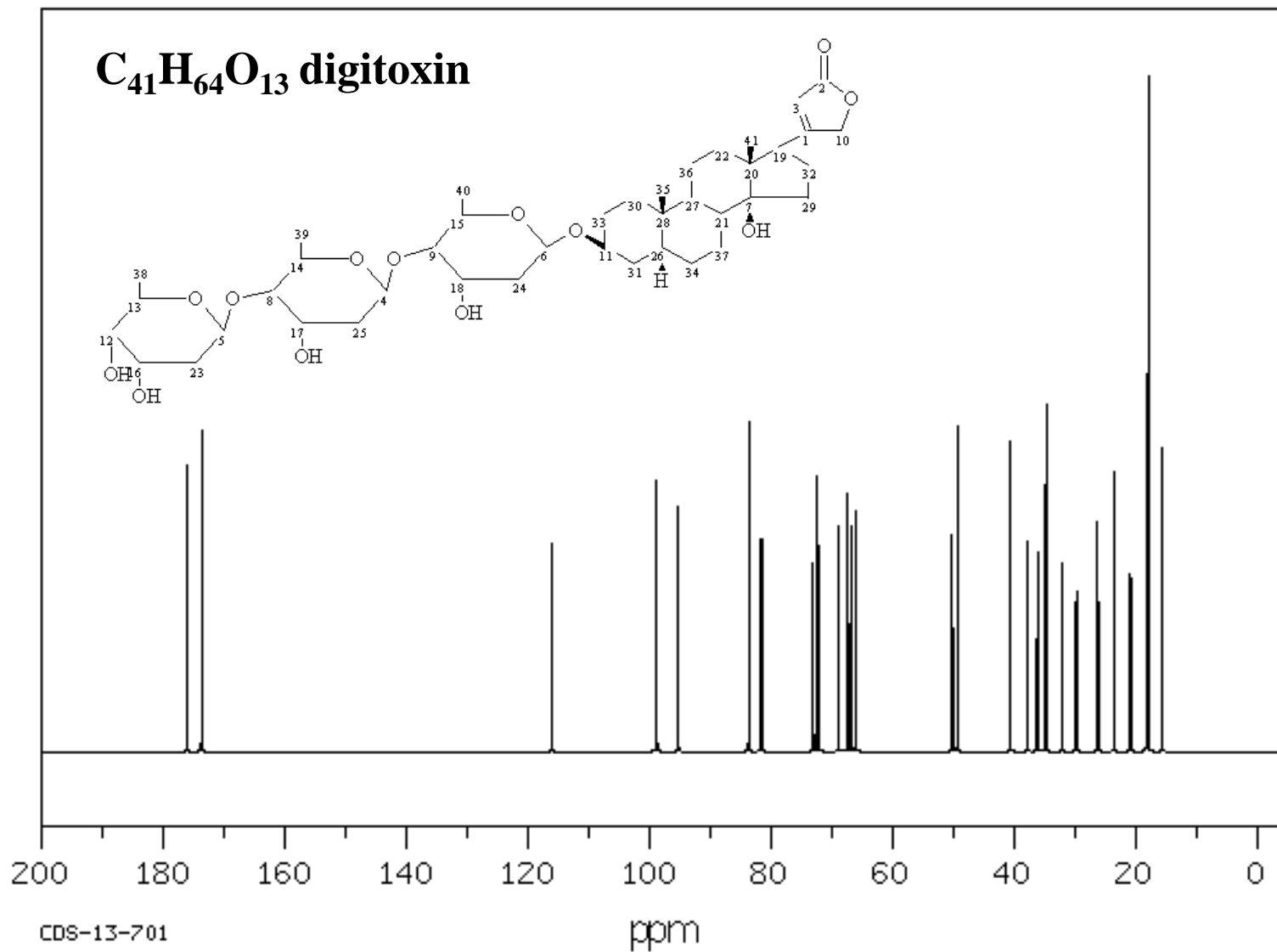
# Espectro de RMN de $^{13}\text{C}$ do citronelol



# Espectro de RMN de $^{13}\text{C}$ da sacarose



50.18 MHz saturated in DMSO-d<sub>6</sub>



SDBS-<sup>13</sup>C NMRSDBS No. 11132CDS-13-701

# Tipos de espectros de RMN de $^{13}\text{C}$

PND (proton noise decoupled)  
ou BBD (broad-band proton decoupled)

(não há acoplamento entre  $^{13}\text{C}$  e  $^1\text{H}$  e cada carbono se apresenta como um singlete)

SFORD: single frequency off resonance decoupled  
(mostra acoplamentos entre  $^{13}\text{C}$  e  $^1\text{H}$ )

C: singlete

CH: dublete

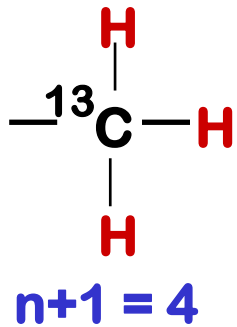
$\text{CH}_2$ : tripleto

$\text{CH}_3$ : quadruplete

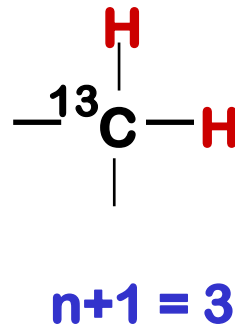
**Atualmente:**

**DEPT** (Distortionless Enhancement by Polarization Transfer) e  
**ed-HSQC** (Heteronuclear single quantum coherence spectroscopy)

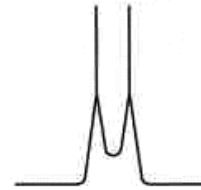
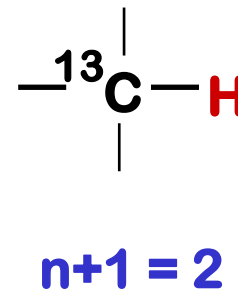
# Mas os $^{13}\text{C}$ não acoplam com os $^1\text{H}$ aos quais estão ligados?



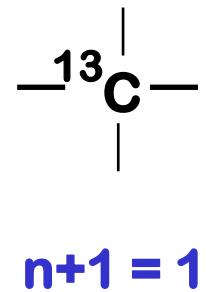
**Methyl**



**Methylene**



**Methine**



**Quaternary**

O efeito no desdobramento de hidrogênios ligados aos  $^{13}\text{C}$  é o mesmo quando se aplica a regra  $n+1$ .

**(J's são da ordem de 100 - 200 Hz)**



# Determinação/identificação de sistemas acoplados em RMN de $^1\text{H}$

## Determinação de J

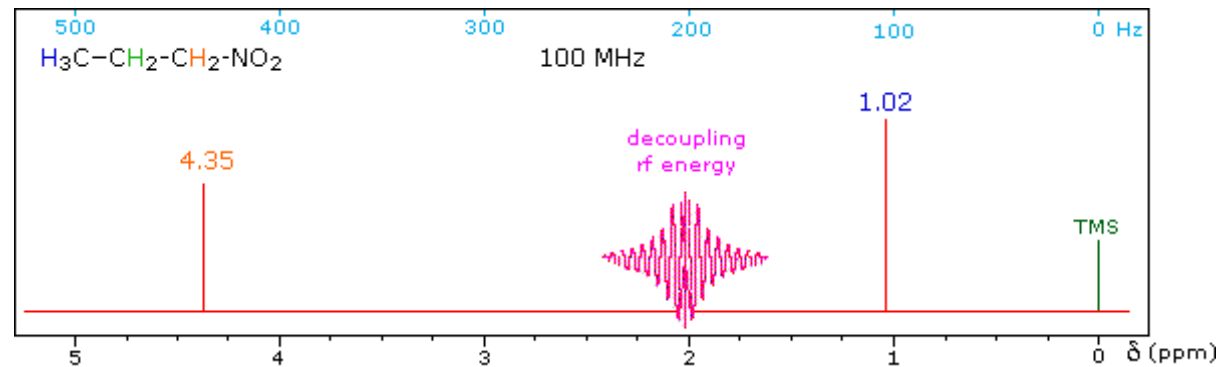
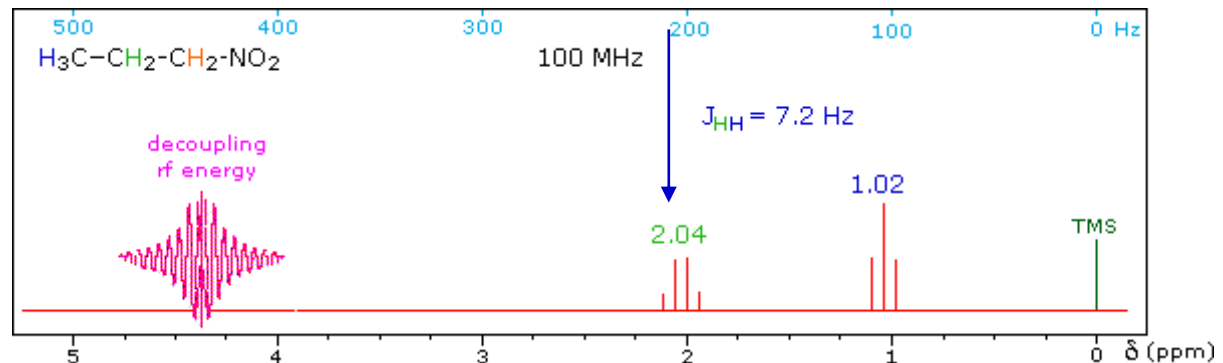
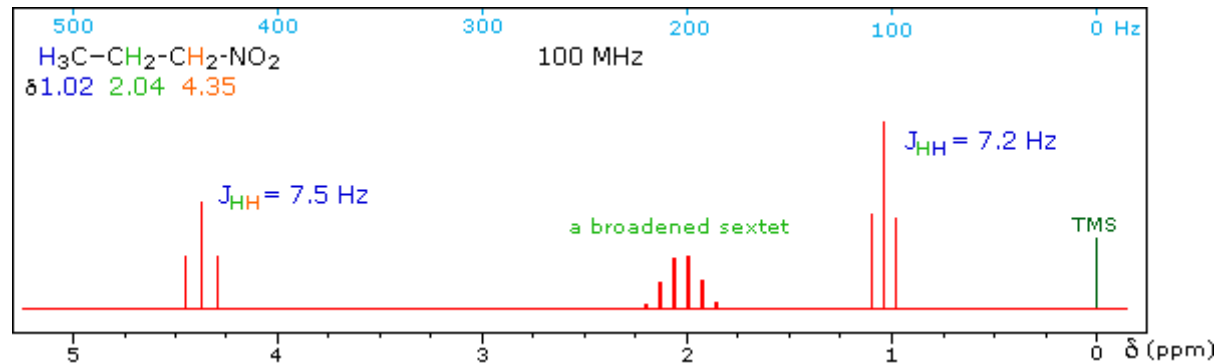
Experimentos de dupla irradiação

COSY (espectro bidimensional)

J resolved (espectro bidimensional)

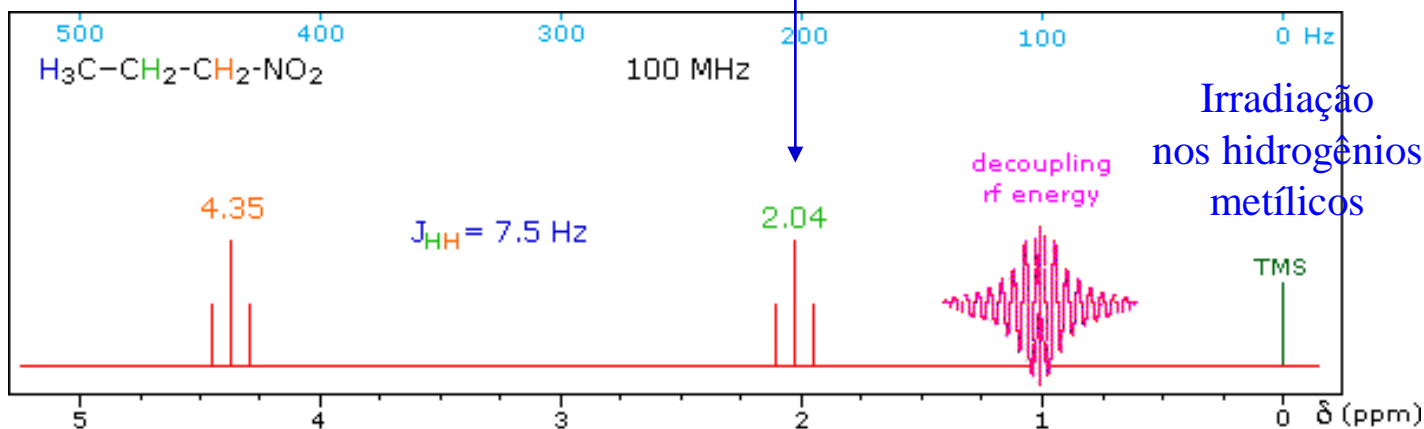
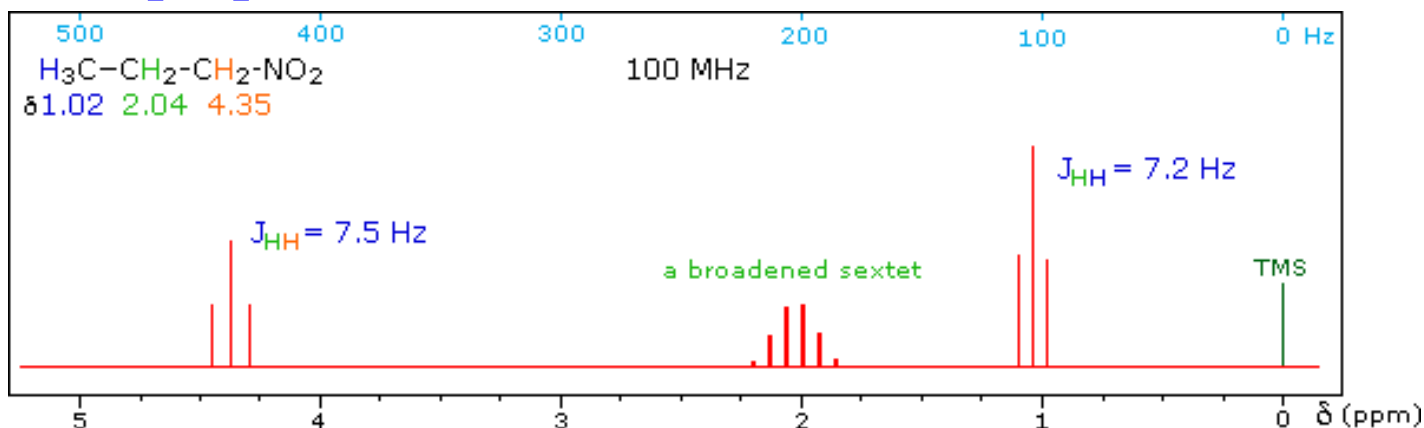
# Experimentos de dupla irradiação em RMN de $^1\text{H}$

nitropropano



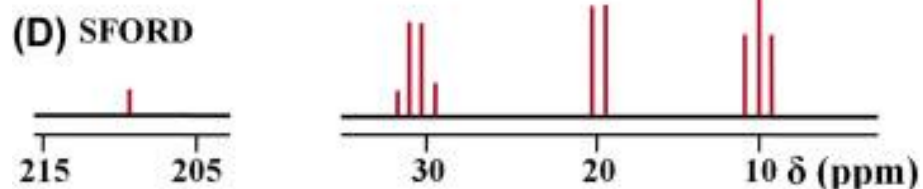
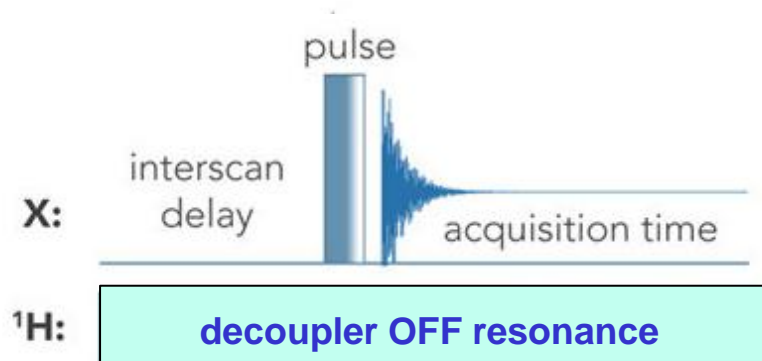
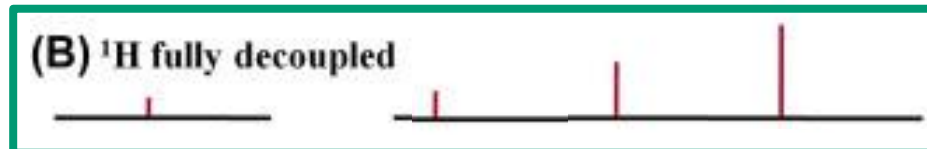
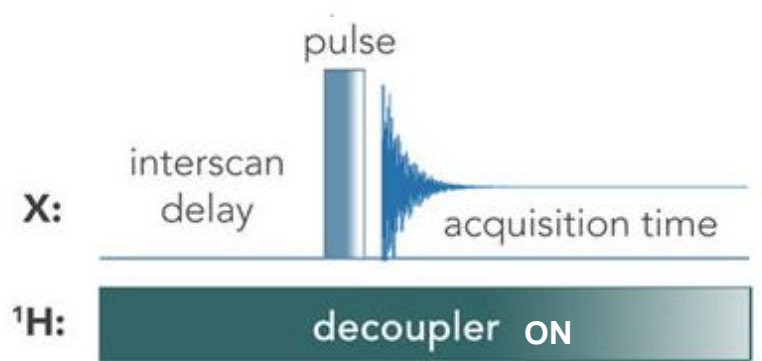
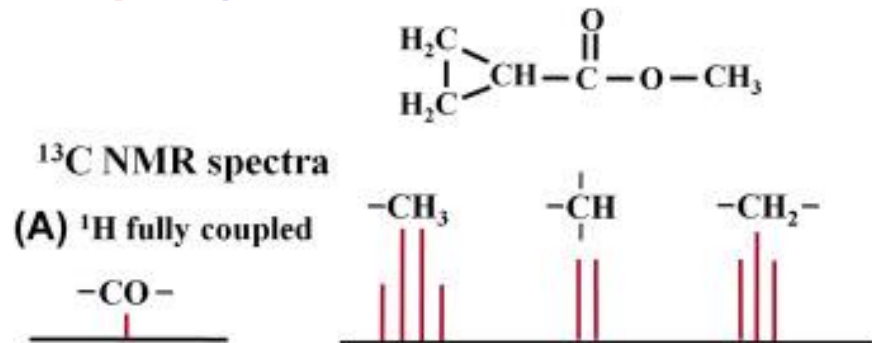
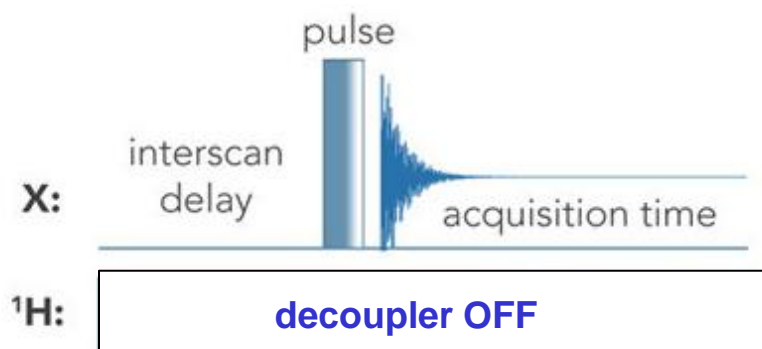
# Experimentos de dupla irradiação em RMN de $^1\text{H}$

nitropropano



O CH<sub>2</sub>-2  
acopla somente  
com o CH<sub>2</sub>-1

Espectros de RMN de  $^{13}\text{C}$  normalmente são totalmente desacoplados de  $^1\text{H}$  (proton noise decoupled, broad band or fully decoupled)



# Efeito nuclear Overhauser (NOE)

Aumento da intensidade dos sinais dos  $^{13}\text{C}$  devido à irradiação nos hidrogênios

$$\text{NOE}_{\text{max}} = \frac{1}{2} \left( \frac{\gamma_{\text{irr}}}{\gamma_{\text{obs}}} \right)$$

$$\text{NOE}_{\text{max}} = \frac{1}{2} \left( \frac{267.5}{67.28} \right) = 1.988$$

Intensidade dos sinais de  $^{13}\text{C}$ :  $\text{CH}_3 > \text{CH}_2 > \text{CH} > \text{C}$

# Mecanismos de relaxamentos

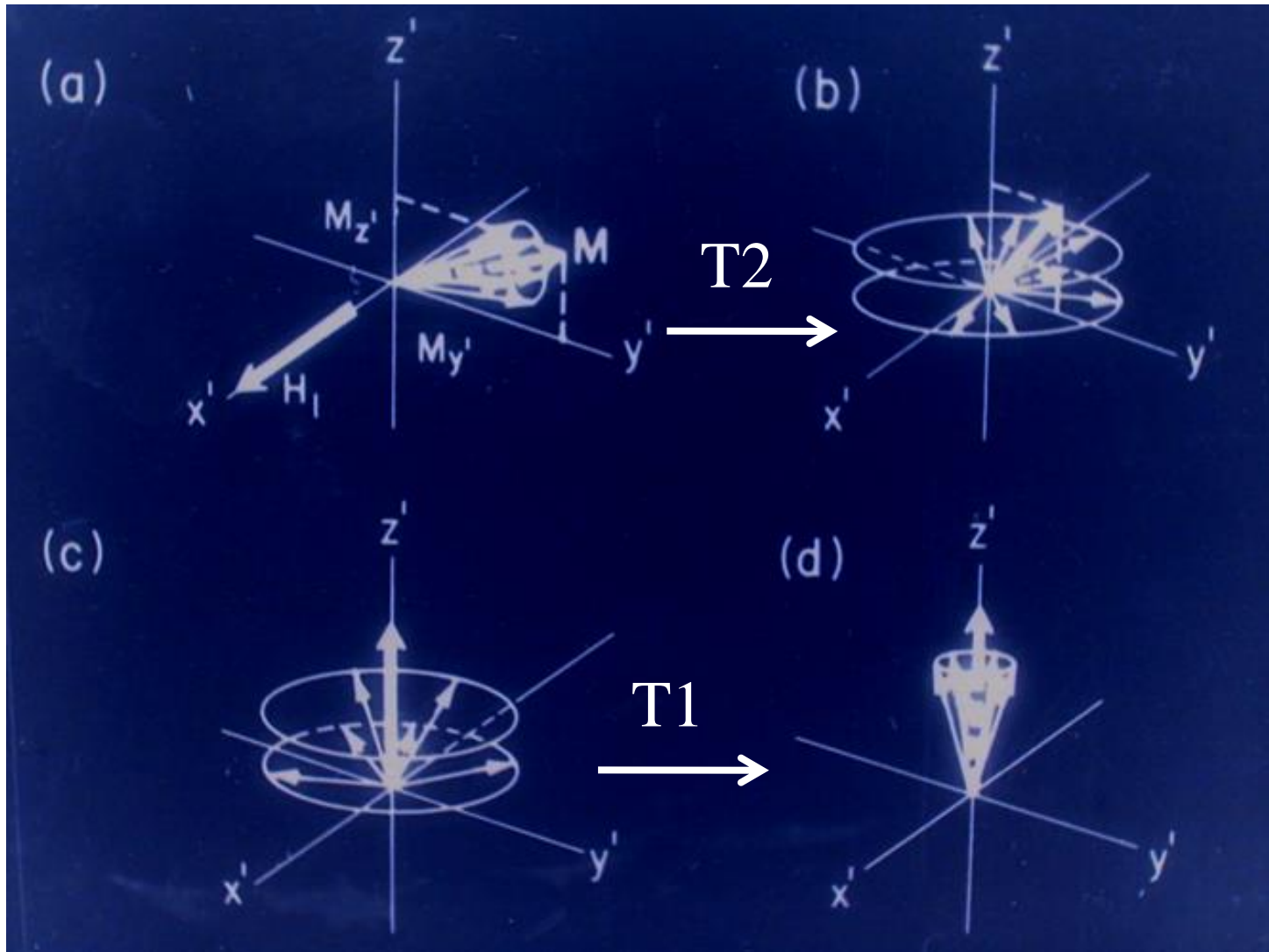
T1 - Relaxamento longitudinal  
(spin-rede/"spin-lattice")

T2 - Relaxamento transversal  
(spin-spin)

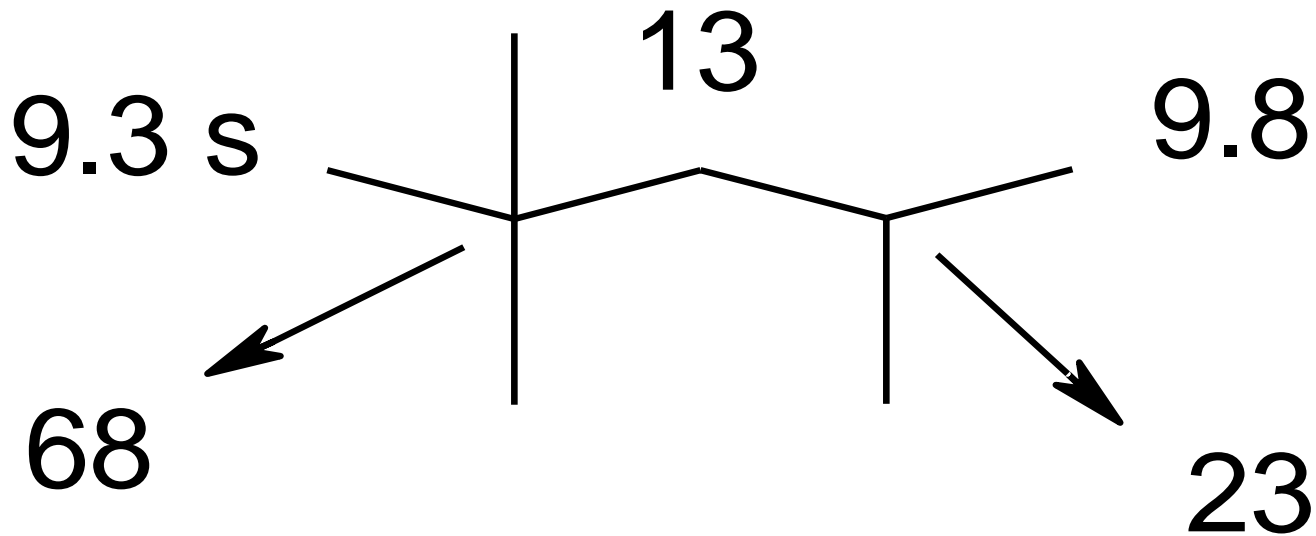
O relaxamento T2 é mais rápido do que T1.

O processo de retorno ao estado a, é constituído pela somatória de T2 + T1.

# Relaxation process (T1 + T2)



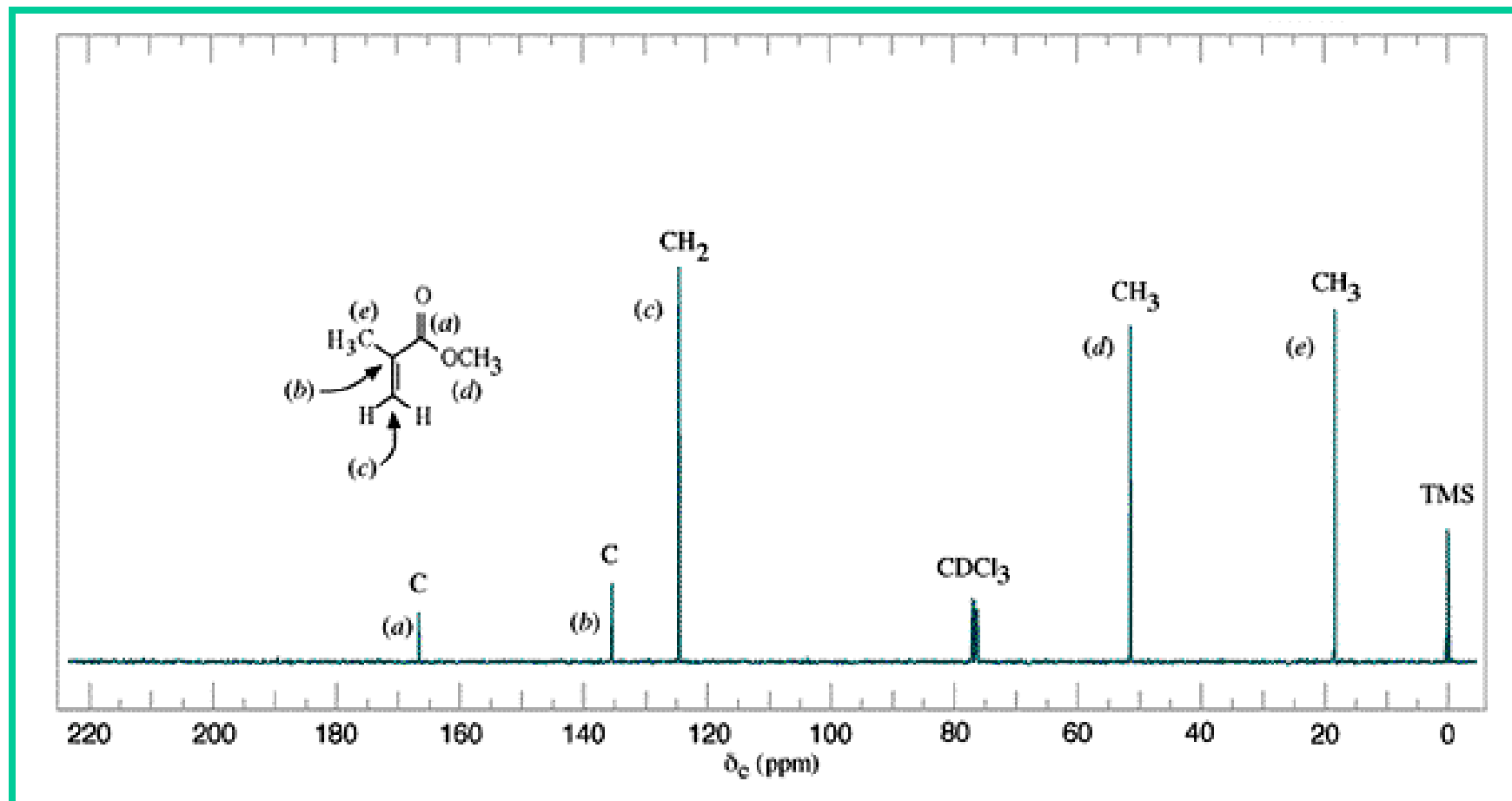
# Tempo de relaxamento longitudinal (T1) (em segundos)



A menor interação dos carbonos quaternários, ou sobre eixos de simetrias, com o meio circundante, faz com que os relaxamentos sejam menos eficientes e a intensidade dos sinais acaba sendo inferior aos carbonos hidrogenados.



# Espectro de RMN de $^{13}\text{C}$ (totalmente desacoplado) do metacrilato de metila

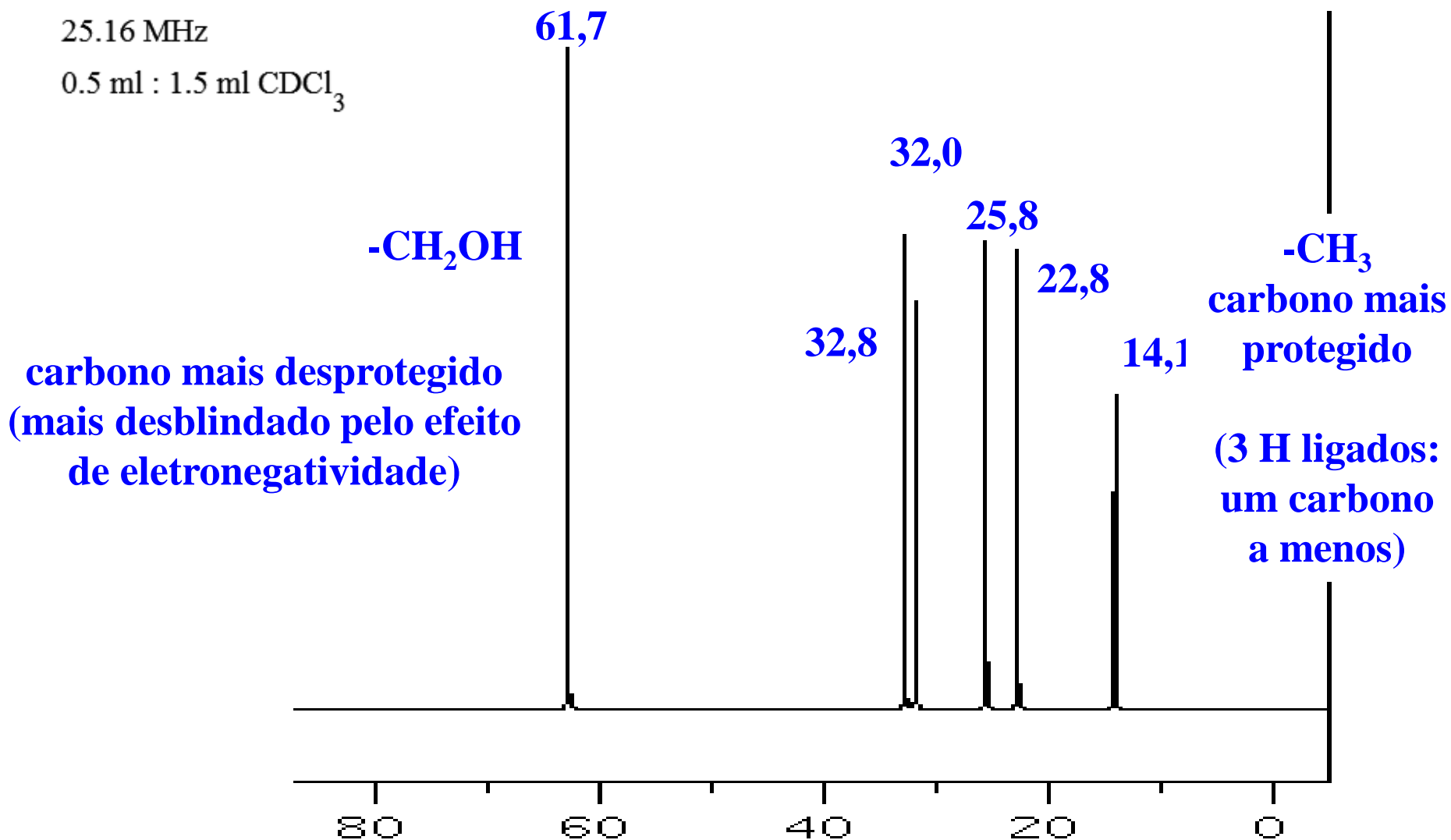


As intensidades dos sinais são variáveis  
(dependem do tempo de relaxamento de cada carbono que quase sempre está  
associado ao número de H ligados aos carbonos)

# Espectro de RMN de $^{13}\text{C}$ do 1-hexanol

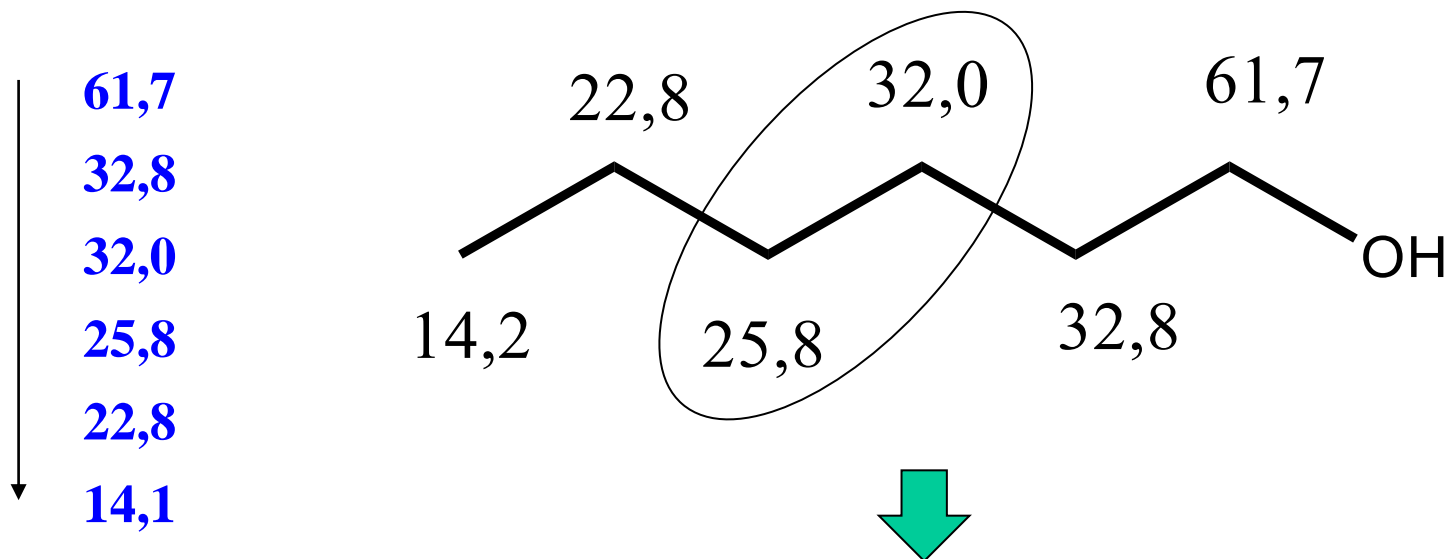
25.16 MHz

0.5 ml : 1.5 ml  $\text{CDCl}_3$

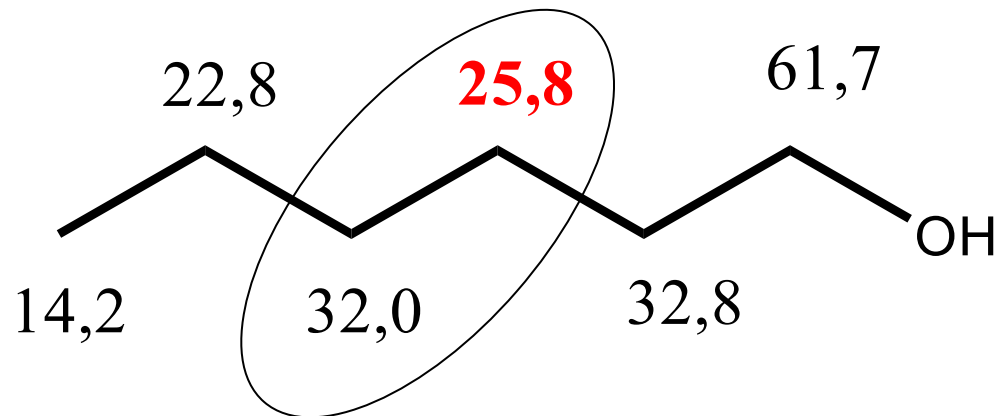


# Atribuição dos sinais de RMN de $^{13}\text{C}$ do 1-hexanol

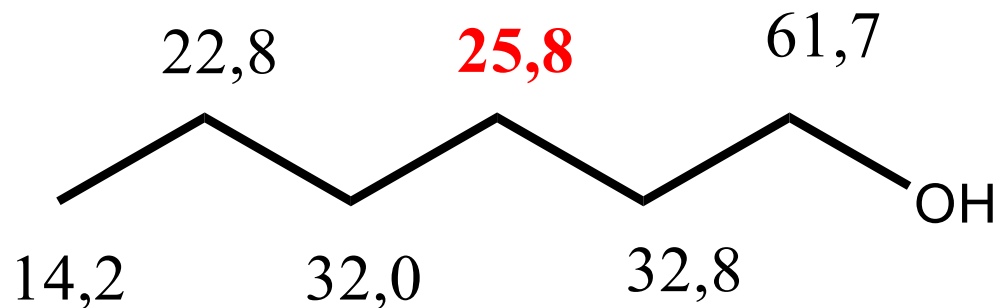
Se for obedecer somente o efeito de eletronegatividade:



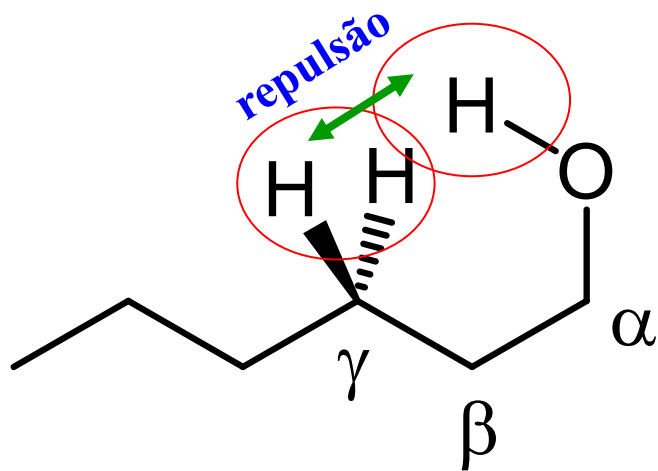
No entanto:



O efeito de eletronegatividade se dispersa ao longo da distância, mas aqui o efeito  $\gamma$  é importante



Efeito gama ( $\gamma$ ): efeito de proteção estérica (-5 ppm)



Com a deformação da ligação C-H, a densidade eletrônica se desloca em direção ao carbono gama.

# Cálculo dos deslocamentos químicos para hidrocarbonetos

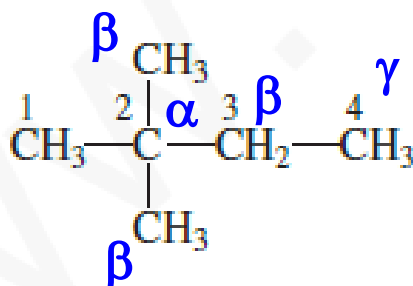


$$\delta_C = -2.3 + 9.1\alpha + 9.4\beta - 2.5\gamma + 0.3\delta + 0.1\epsilon + \Sigma (\text{steric corrections}) \text{ ppm}$$

Steric Corrections (ppm)				
Carbon Atom Observed	Type of Carbons Attached			
	Primary	Secondary	Tertiary	Quaternary
Primary	0	0	-1.1	-3.4
Secondary	0	0	-2.5	-7.5
Tertiary	0	-3.7	-8.5	-10.0
Quaternary	-1.5	-8.4	-10.0	-12.5

Steric Corrections (ppm)				
Carbon Atom Observed	Type of Carbons Attached			
	Primary	Secondary	Tertiary	Quaternary
Primary	0	0	-1.1	-3.4
Secondary	0	0	-2.5	-7.5
Tertiary	0	-3.7	-8.5	-10.0
Quaternary	-1.5	-8.4	-10.0	-12.5

$$\delta_C = -2.3 + 9.1\alpha + 9.4\beta - 2.5\gamma + 0.3\delta + 0.1\epsilon + \Sigma (\text{steric corrections}) \text{ ppm}$$



2,2-Dimethylbutane

<i>Actual values:</i>	C1	29.1 ppm
	C2	30.6 ppm
	C3	36.9 ppm
	C4	8.9 ppm

$$C1 = -2.3 + 9.1(1) + 9.4(3) - 2.5(1) + 0.3(0) + 0.1(0) + [1(-3.4)] = 29.1 \text{ ppm}$$

Steric correction (boldface) = primary with 1 adjacent quaternary

$$C2 = -2.3 + 9.1(4) + 9.4(1) - 2.5(0) + 0.3(0) + 0.1(0) + [3(-1.5)] + [1(-8.4)] = 30.6 \text{ ppm}$$

Steric corrections = quaternary/3 adj. primary, and quaternary/1 adj. secondary

$$C3 = -2.3 + 9.1(2) + 9.4(3) - 2.5(0) + 0.3(0) + 0.1(0) + [1(0)] + [1(-7.5)] = 36.6 \text{ ppm}$$

Steric corrections = secondary/1 adj. primary, and secondary/1 adj. quaternary

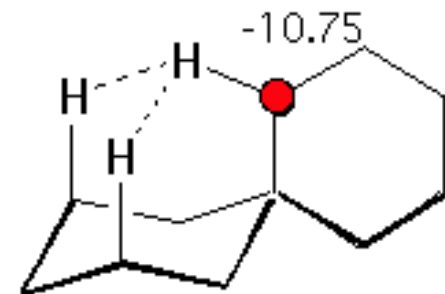
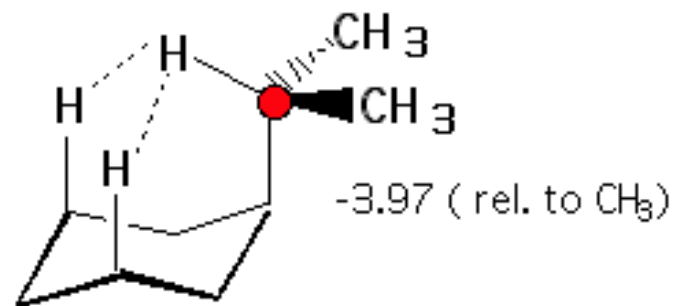
$$C4 = -2.3 + 9.1(1) + 9.4(1) - 2.5(3) + 0.3(0) + 0.1(0) + [1(0)] = 8.7 \text{ ppm}$$

Steric correction = primary/1 adj. secondary

# Efeito gama: efeito de proteção estérica (-5 ppm)

## Steric effects

- The more rigid the structure, the greater the steric interference and the greater the shielding effect



- The more such interactions, the greater the shielding

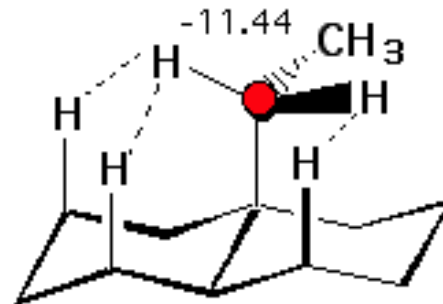


TABLE A 8.3

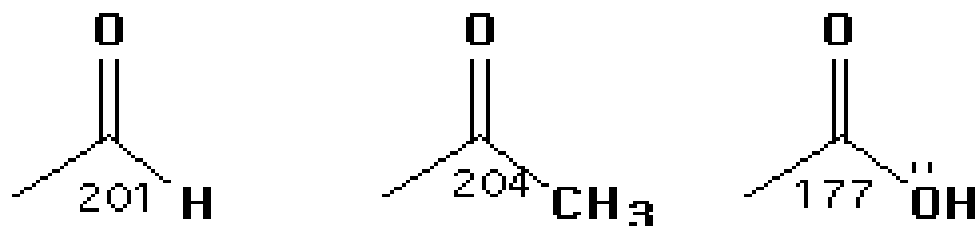
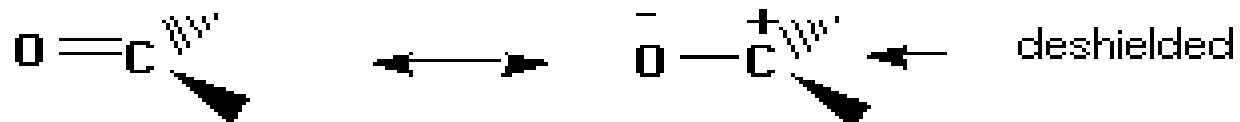
<sup>13</sup>C SUBSTITUENT INCREMENTS FOR ALKANES AND CYCLOALKANES (PPM)<sup>a</sup>

Substituent Y	Terminal: $Y-C_{\alpha}-C_{\beta}-C_{\gamma}$			Internal: $C_{\gamma}-C_{\beta}-C_{\alpha}-C_{\beta}-C_{\gamma}$		
	$\alpha$	$\beta$	$\gamma$	$\alpha$	$\beta$	$\gamma$
-D	-0.4	-0.1	0			
-CH <sub>3</sub>	9	10	-2	6	8	-2
-CH=CH <sub>2</sub>	19.5	6.9	-2.1			-0.5
-C≡CH	4.5	5.4	-3.5			-3.5
-C <sub>6</sub> H <sub>5</sub>	22.1	9.3	-2.6	17	7	-2
-CHO	29.9	-0.6	-2.7			
-COCH <sub>3</sub>	30	1	-2	24	1	-2
-COOH	20.1	2	-2.8	16	2	-2
-COOR	22.6	2	-2.8	17	2	-2
-CONH <sub>2</sub>	22	2.5	-3.2			-0.5
-CN	3.1	2.4	-3.3	1	3	-3
-NH <sub>2</sub>	29	11	-5	24	10	-5
-NHR	37	8	-4	31	6	-4
-NR <sub>2</sub>	42	6	-3			-3
-NO <sub>2</sub>	61.6	3.1	-4.6	57	4	
-OH	48	10	-6.2	41	8	-5
-OR	58	8	-4	51	5	-4
-OCOCH <sub>3</sub>	56.5	6.5	-6.0	45	5	-3
-F	70.1	7.8	-6.8	63	6	-4
-Cl	31	10	-5.1	32	10	-4
-Br	20	11	-3	25	10	-3
-I	-7.2	10.9	-1.5	4	12	-1

<sup>a</sup>Add these increments to the values given in Table A8.1.

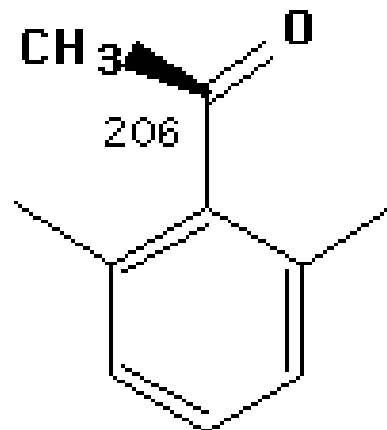
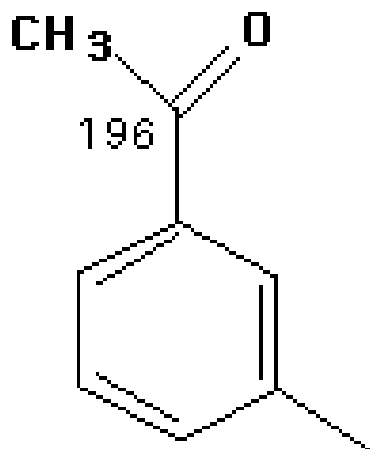
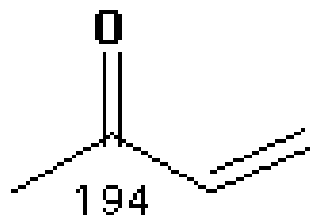
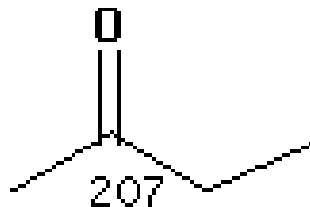


# O efeito da hibridização e dos efeitos de substituintes sobre os deslocamento químicos dos carbonos



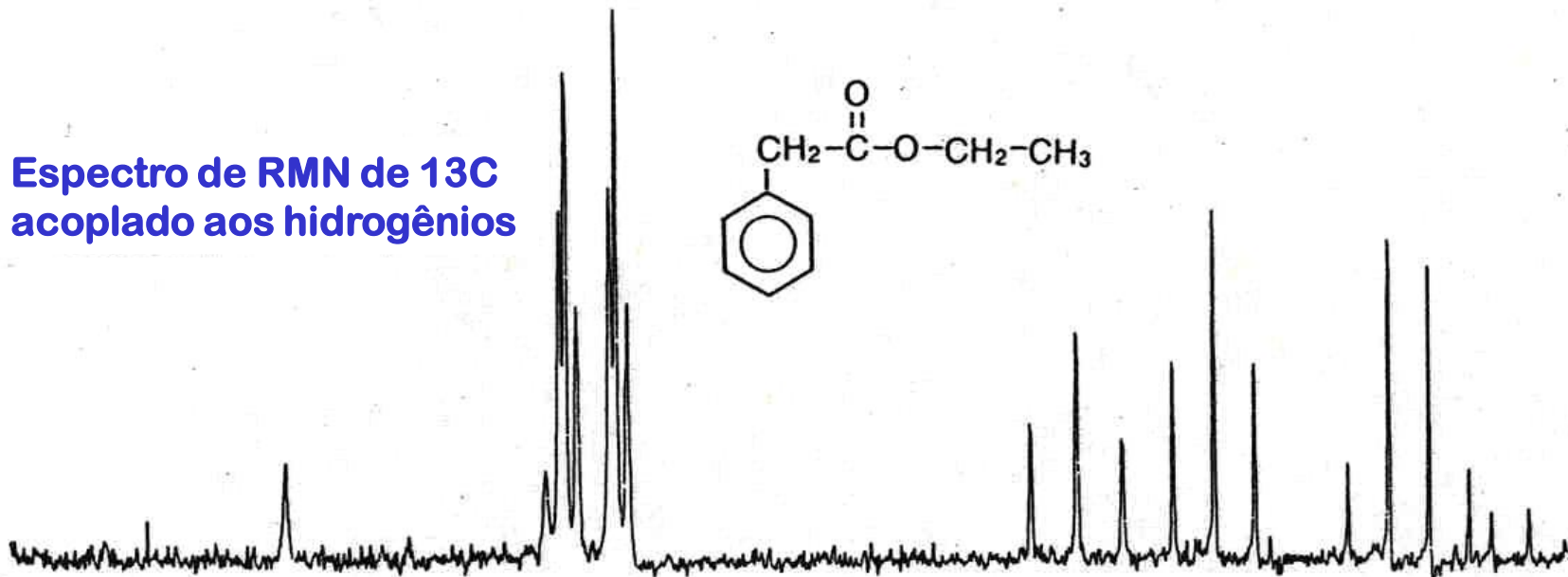
positive charge delocalised away from carbon

# O efeito da conjugação sobre o deslocamento químico dos carbonos

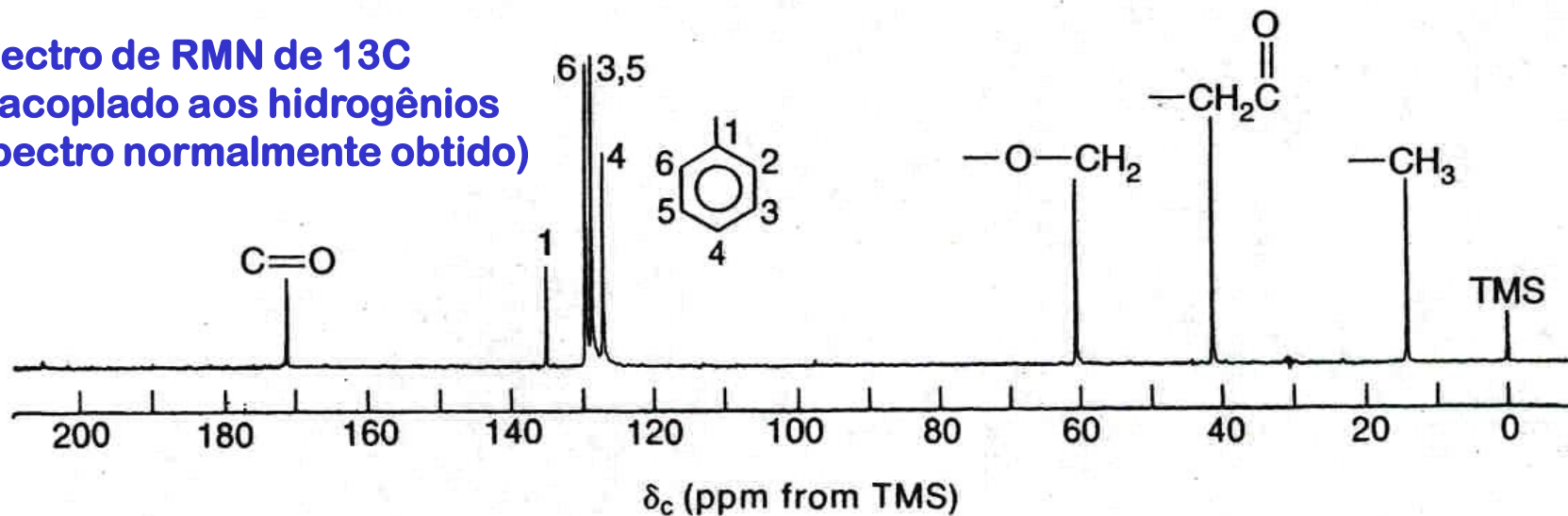


# Espectro de RMN do fenilacetato de etila

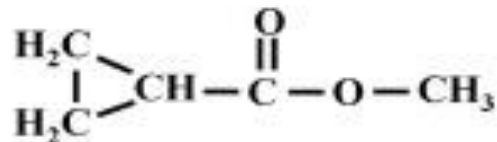
Espectro de RMN de  $^{13}\text{C}$   
acoplado aos hidrogênios



Espectro de RMN de  $^{13}\text{C}$   
desacoplado aos hidrogênios  
(espectro normalmente obtido)

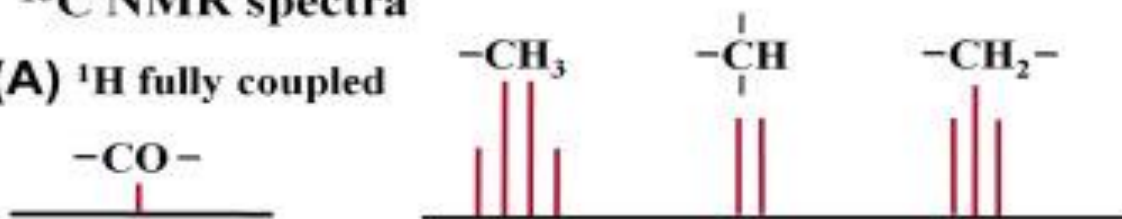


A informação sobre o tipo de carbono  
(C, CH, CH<sub>2</sub> e CH<sub>3</sub>) são atualmente obtidos por DEPT  
(Distortionless Enhancement by Polarization Transfer)



<sup>13</sup>C NMR spectra

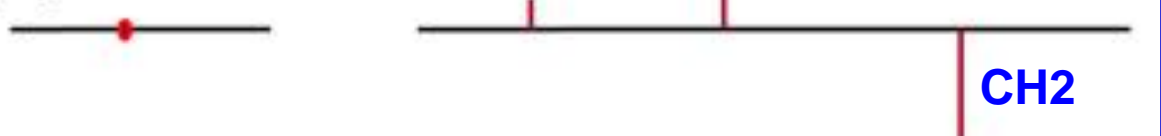
(A) <sup>1</sup>H fully coupled



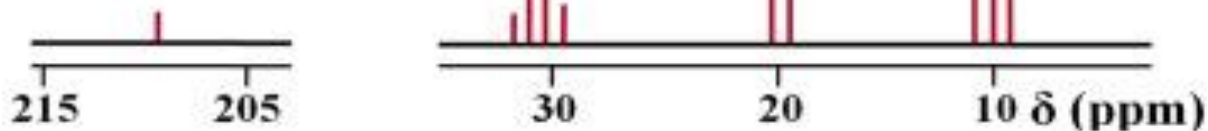
(B) <sup>1</sup>H fully decoupled



(C) DEPT



(D) SFORD



215 205

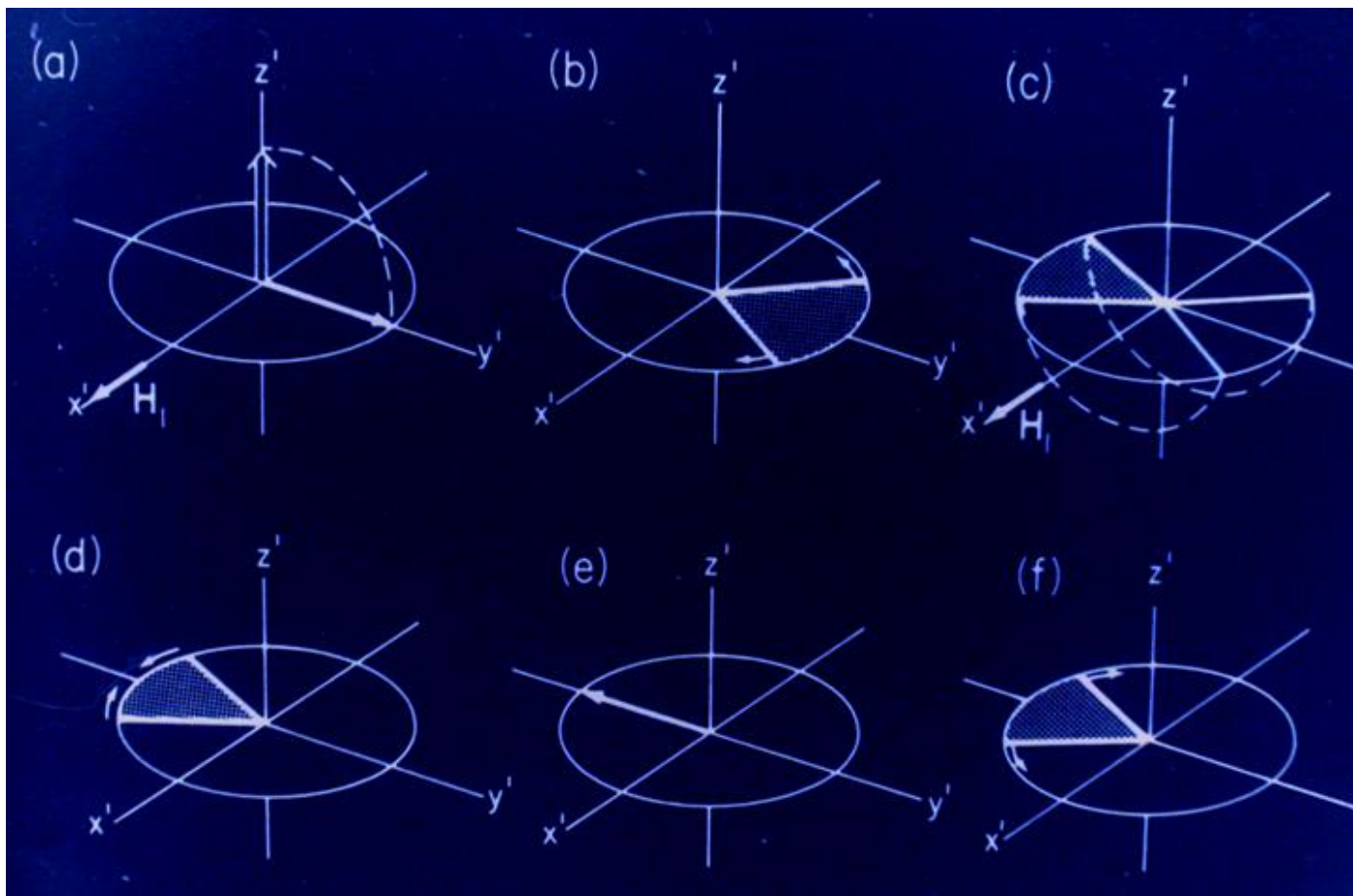
30

20

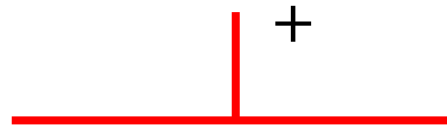
10 δ (ppm)

# Determinação de T2 – Método do eco de spin (Hahn)

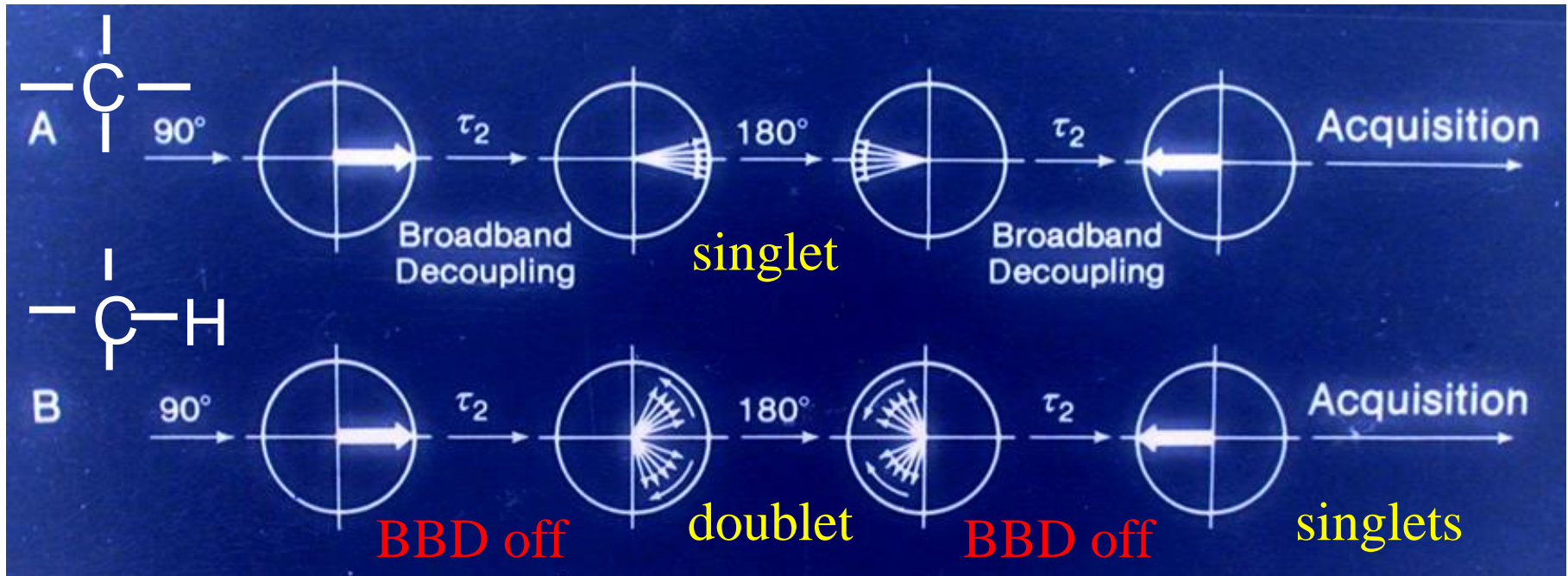
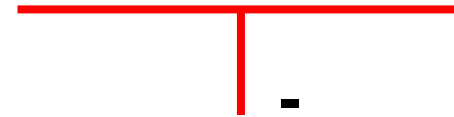
Sequencia de pulsos:  $90_x^\circ - \tau - 180_x^\circ$  ( $\tau=0.1-1$  s)



# As sequencias de pulsos semelhantes do método do eco de spin podem gerar sinais negativos



$^{13}\text{C}$  NMR signals



Delay Time,  $\tau_2$

$1/4J$

$1/2J$

$3/4J$

$1/J$

**C**

Singlet



**CH**

Doublet



**CH<sub>2</sub>**

Triplet

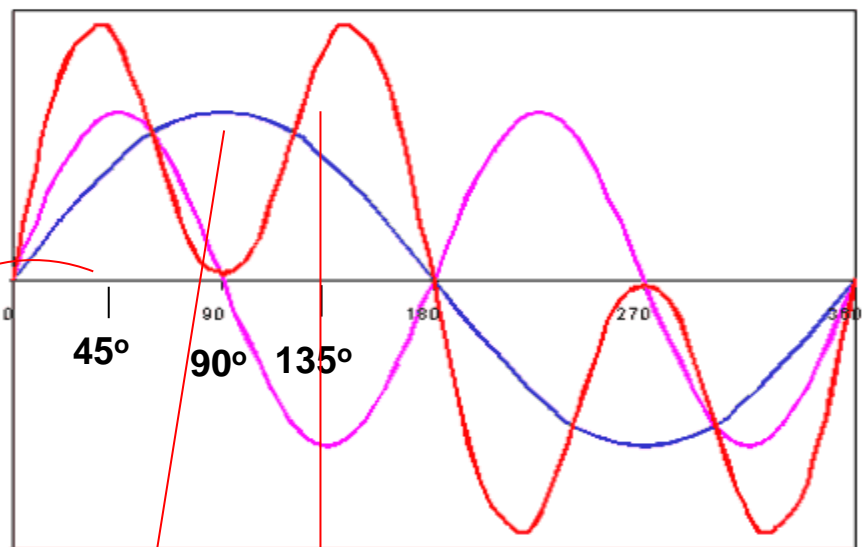


**CH<sub>3</sub>**

Quartet

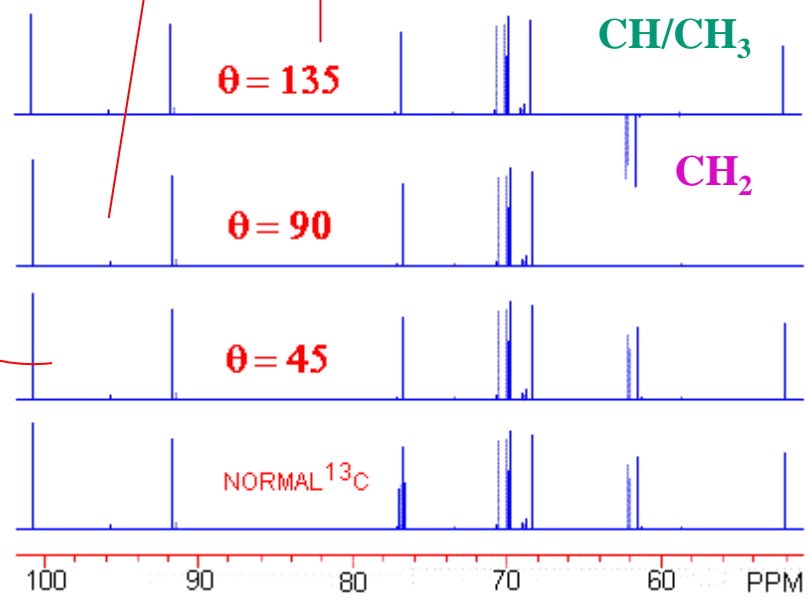


# DEPT : Distortionless Enhancement by Polarization Transfer



- CH  $\Rightarrow \sin(\theta)$
- CH<sub>2</sub>  $\Rightarrow 2\sin(\theta) + \cos(\theta)$
- CH<sub>3</sub>  $\Rightarrow 4\sin(\theta) + \cos^2(\theta)$

**DEPT experiment**



CH up, CH<sub>2</sub> down, CH<sub>3</sub> up

Only singly protonated carbons shows up : CH up

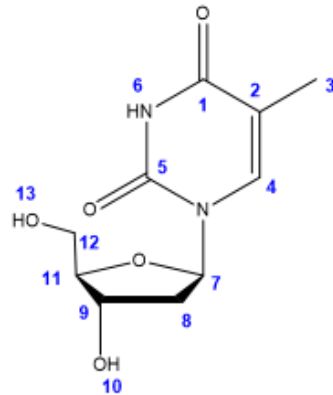
All protonated carbons shows up (no quaternary & no deuterated solvent - CDCl<sub>3</sub> absent!)

**CH +**

**Todos protonados e os quaternários não aparecem.**



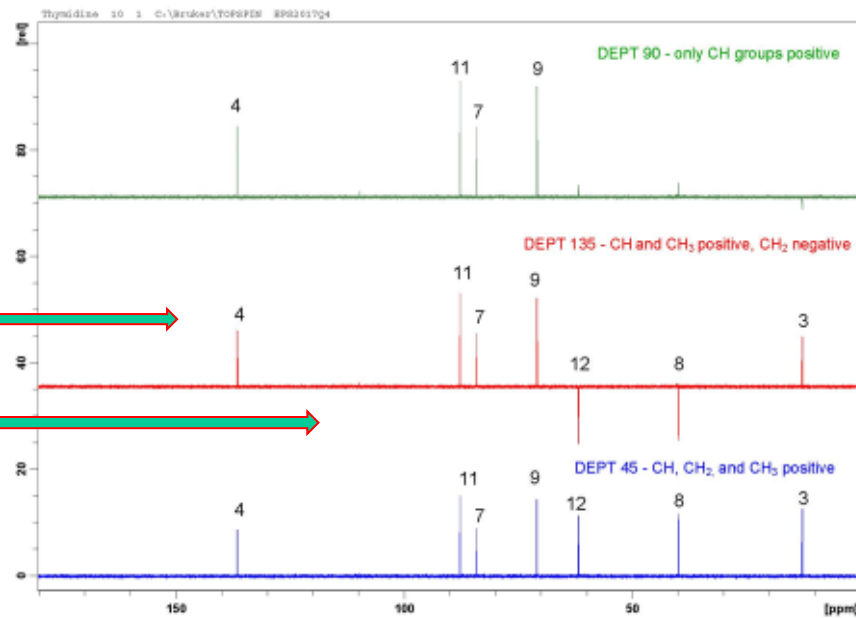
# Espectro DEPT para a timidina



sinais de CH e CH<sub>3</sub>  
positivos

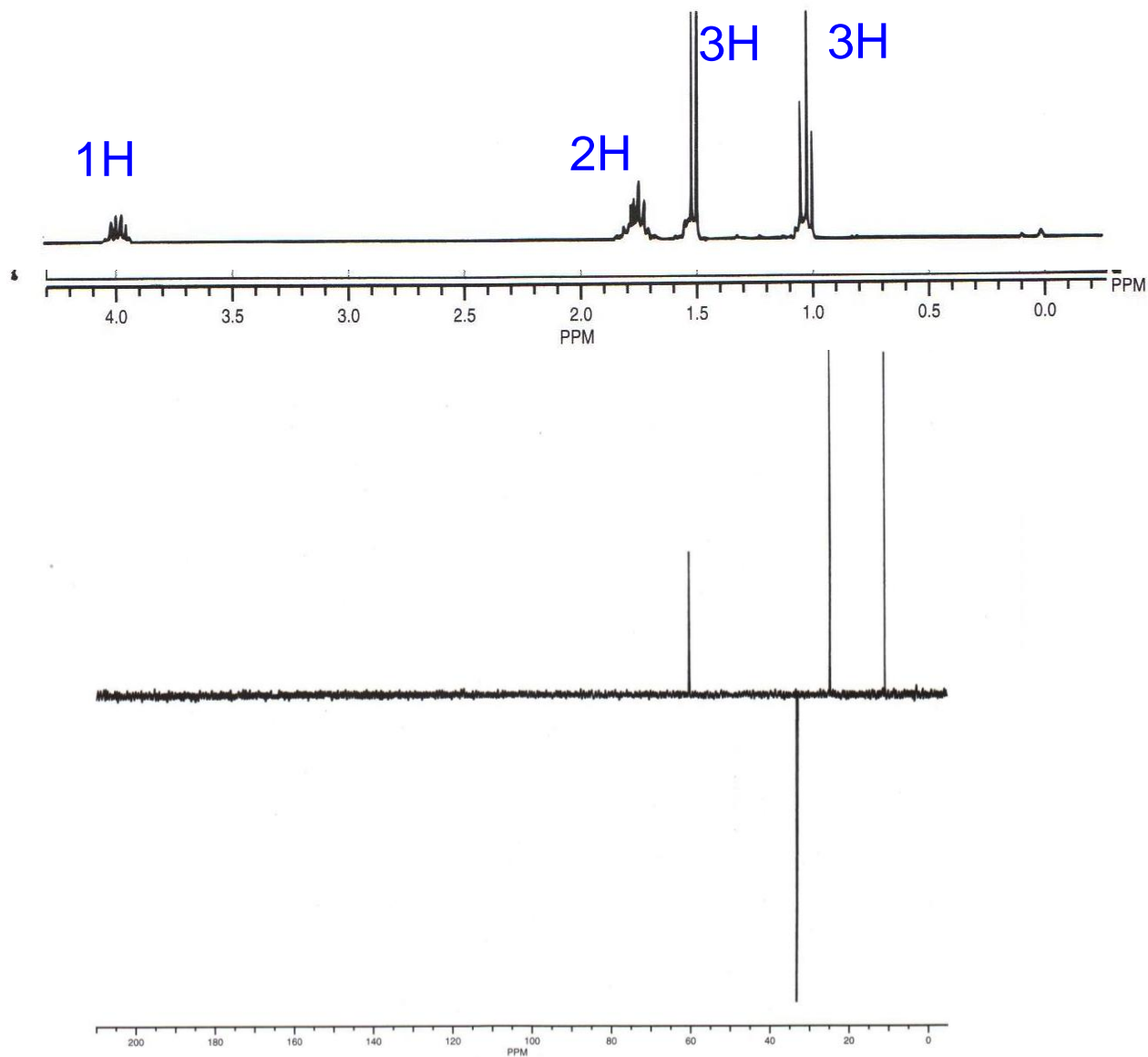
sinais de CH<sub>2</sub>  
negativos

Apenas C  
hidrogenados  
(quaternários não  
Aparecem)

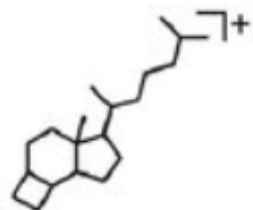


Experiment	C	CH	CH <sub>2</sub>	CH <sub>3</sub>
DEPT-45	not visible	positive	positive	positive
DEPT-90	not visible	positive	not visible	not visible
DEPT-135	not visible	positive	negative	positive

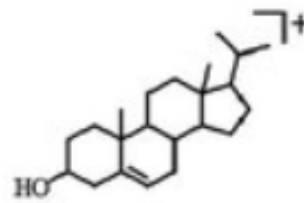
Com base nos espectros de RMN de  $^1\text{H}$  e DEPT 135, determine a estrutura do composto que possui formula molecular  $\text{C}_4\text{H}_9\text{Cl}$



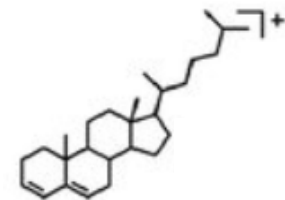
# Espectro de massas (IE) do colesterol



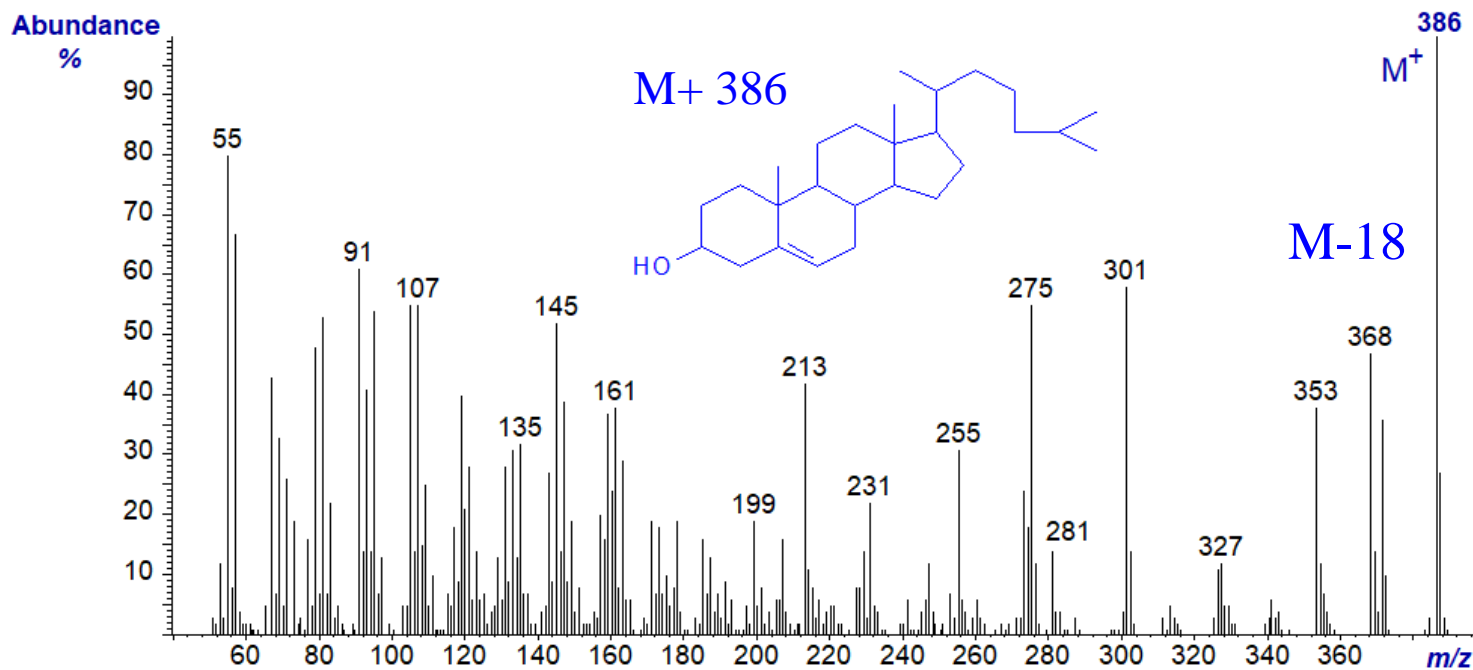
m/z 275



m/z 301



m/z 368



# Espectro UV e IV do colesterol

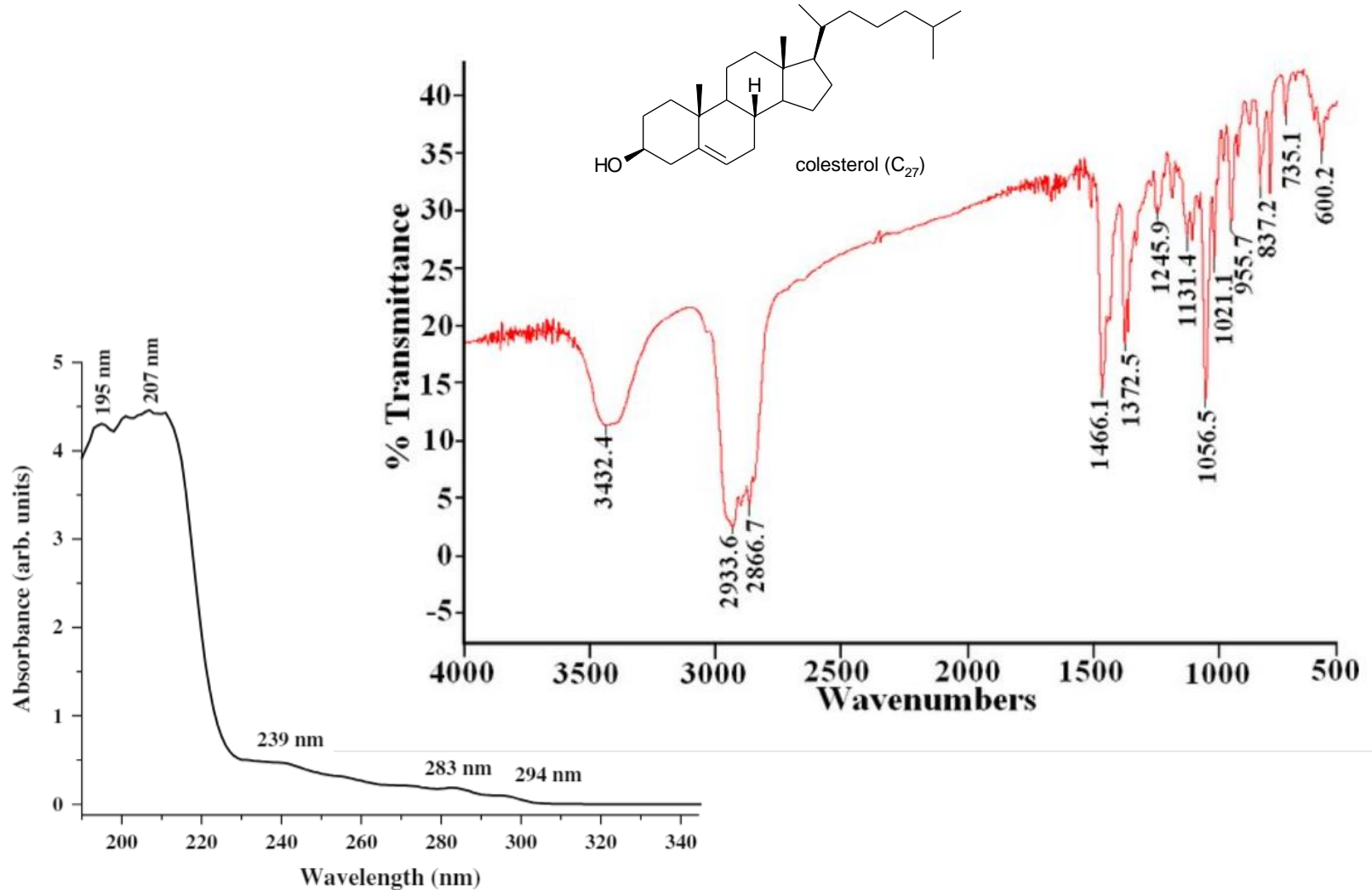
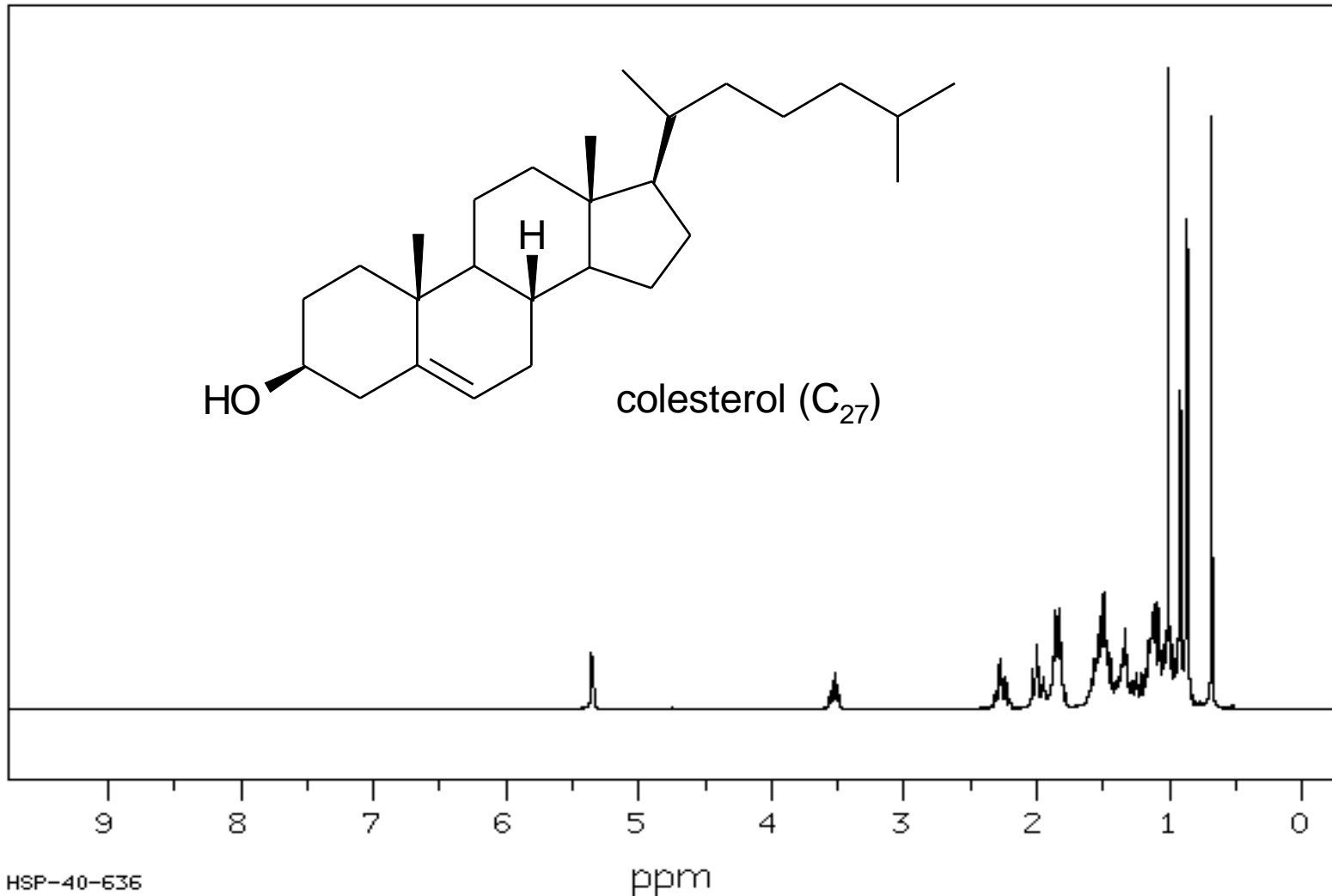


Fig. 4. UV-vis spectrum of Cholesterol.

# Espectro de RMN $^1\text{H}$ do colesterol

O que você consegue atribuir ?



# Espectro de RMN de $^{13}\text{C}$ do colesterol

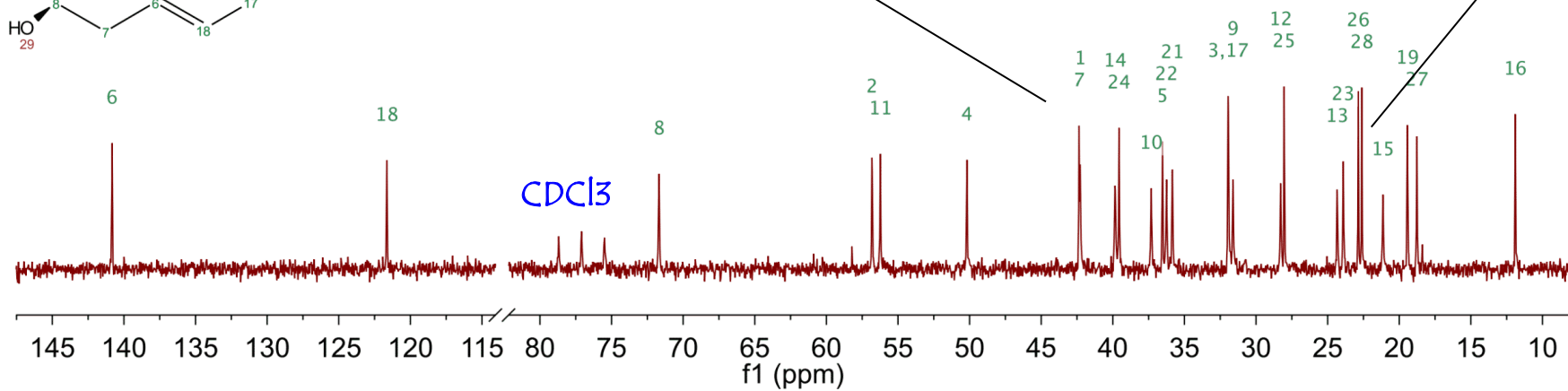
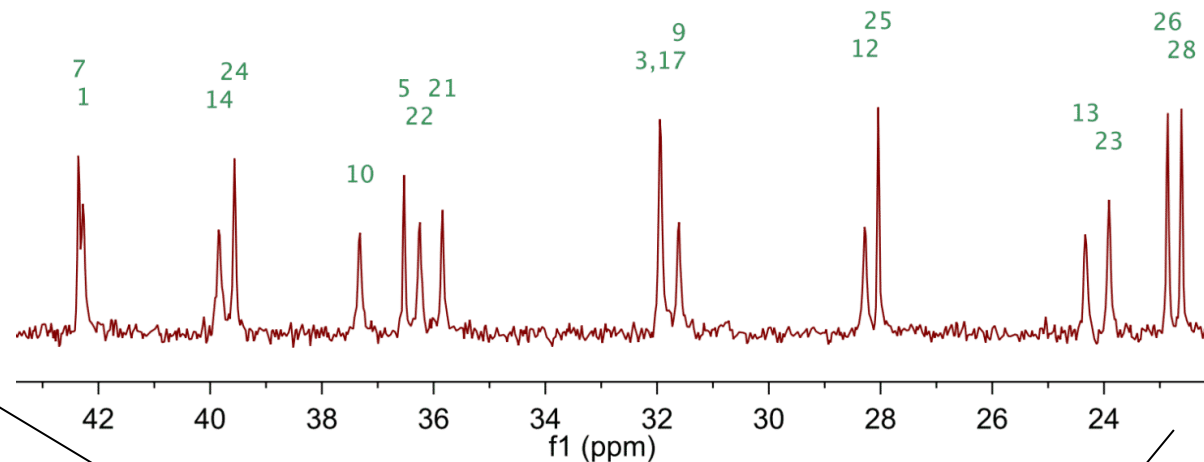
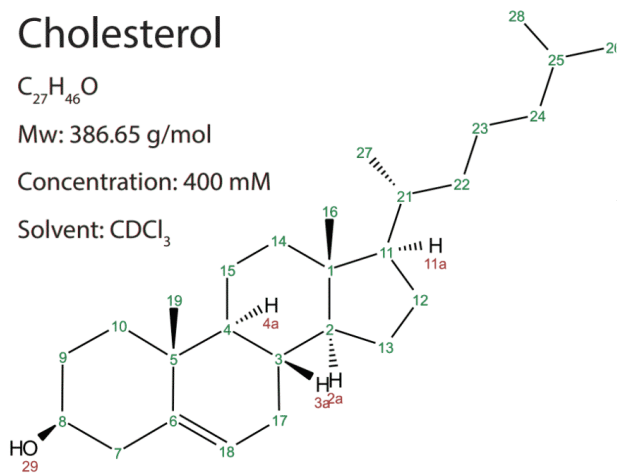
## Cholesterol

$\text{C}_{27}\text{H}_{46}\text{O}$

Mw: 386.65 g/mol

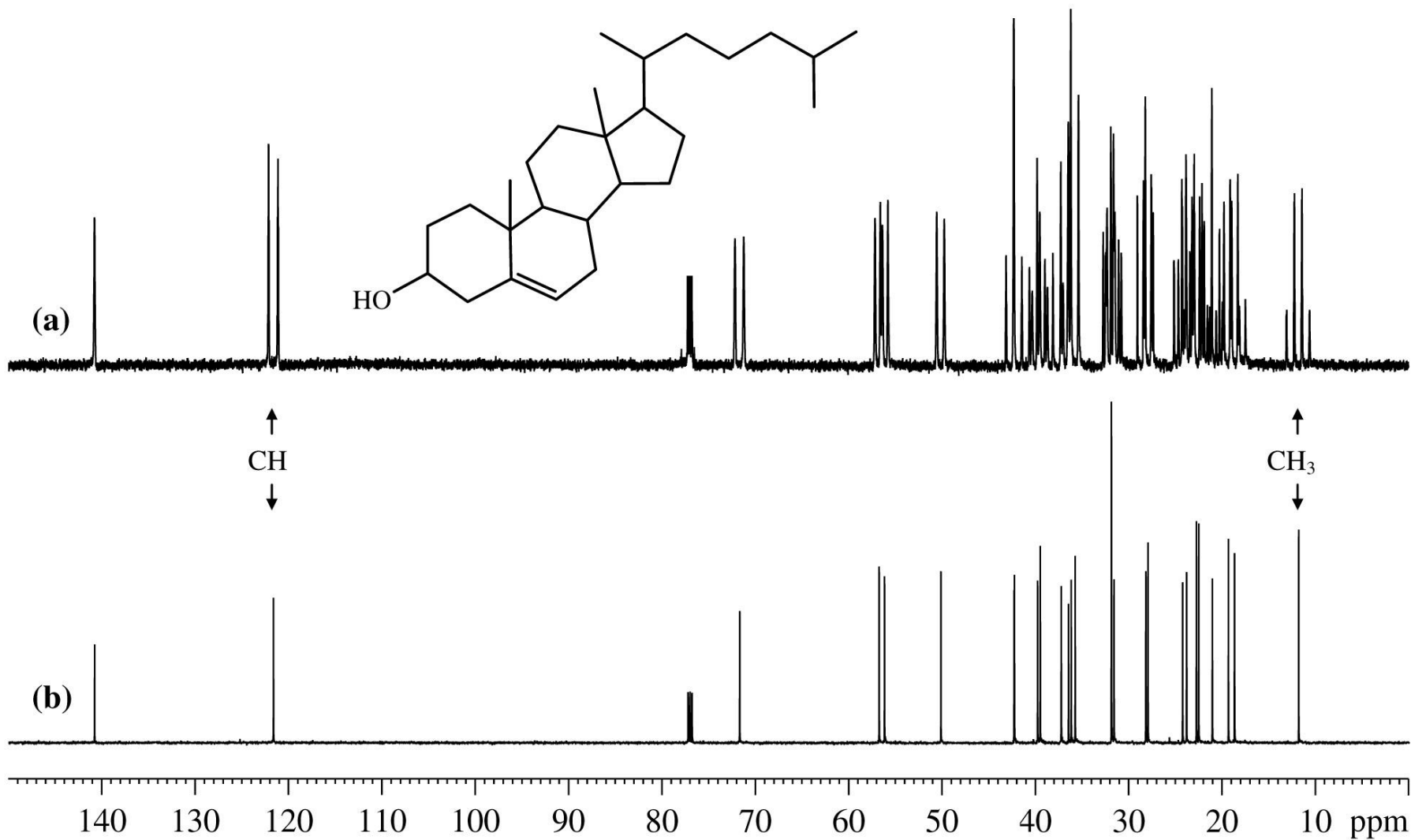
Concentration: 400 mM

Solvent:  $\text{CDCl}_3$

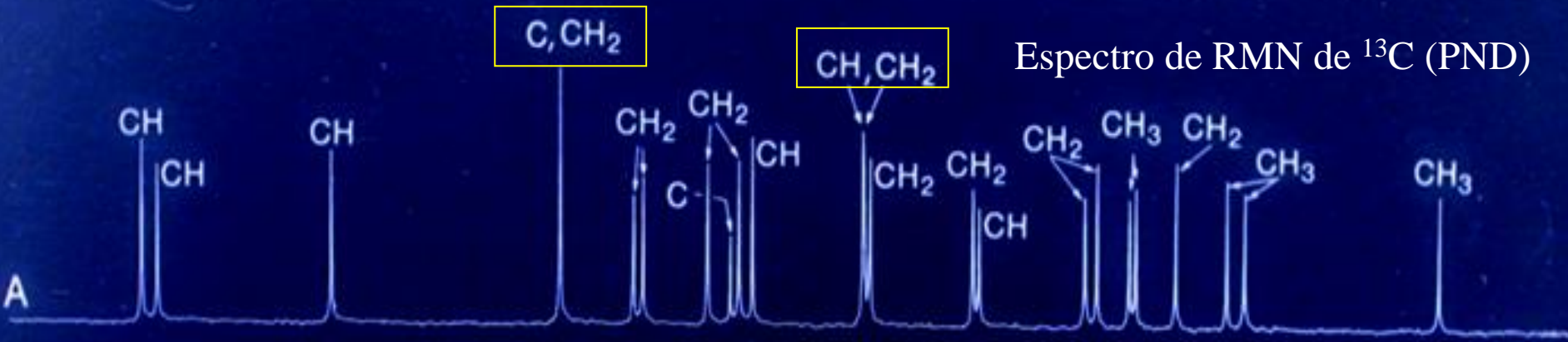


# Espectros de RMN de $^{13}\text{C}$ parcialmente acoplados

J para C-H  $\sim 110\text{-}300$  Hz (C-C-H e C-C-C-H são de  $0\text{-}60$  Hz)



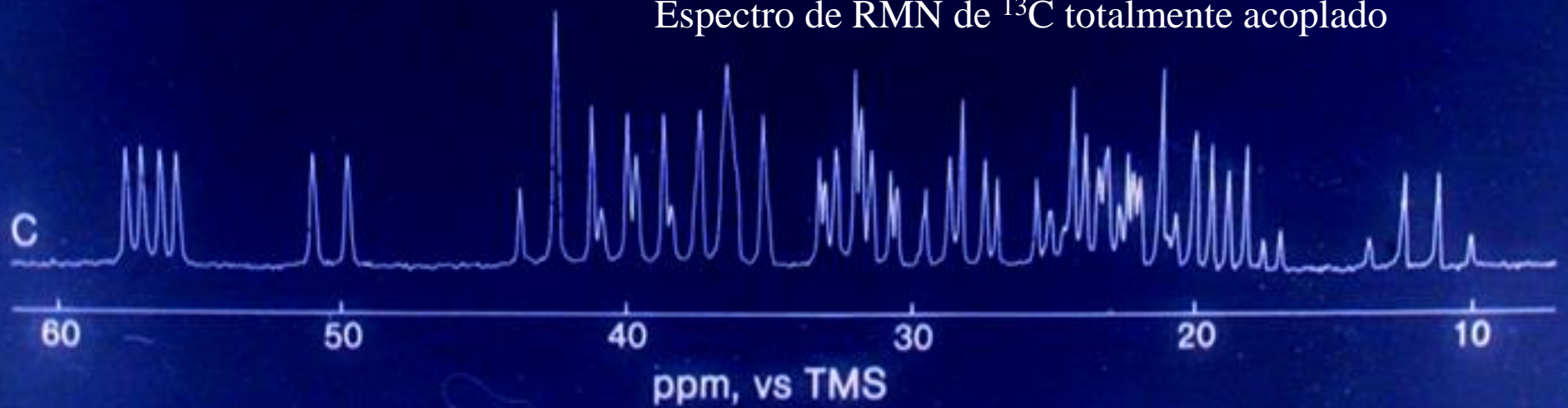
Espectro de RMN de  $^{13}\text{C}$  (PND)



Espectro de RMN de  $^{13}\text{C}$   
SFORD (com acoplamento residual)

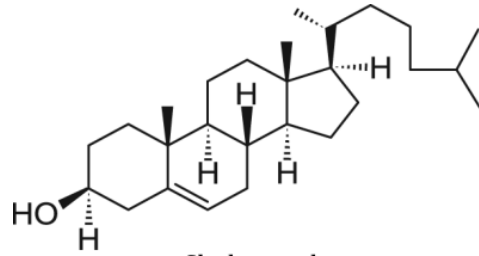


Espectro de RMN de  $^{13}\text{C}$  totalmente acoplado

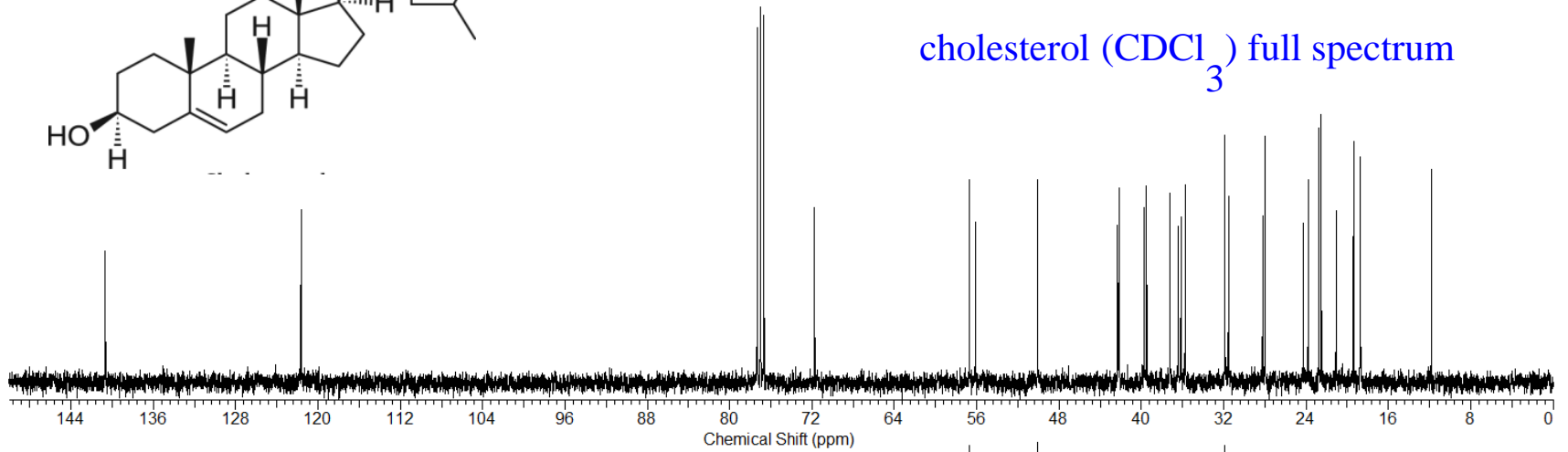




# $^{13}\text{C}$ NMR spectra of cholesterol

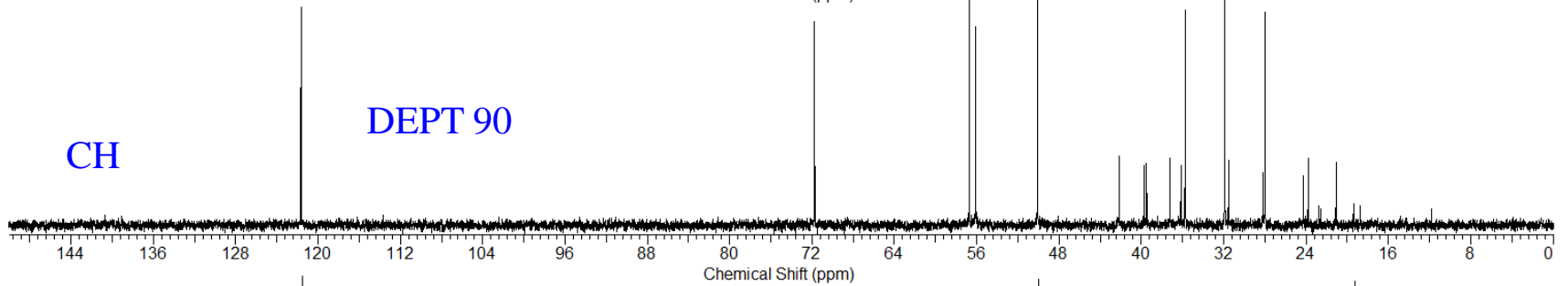


cholesterol ( $\text{CDCl}_3$ ) full spectrum



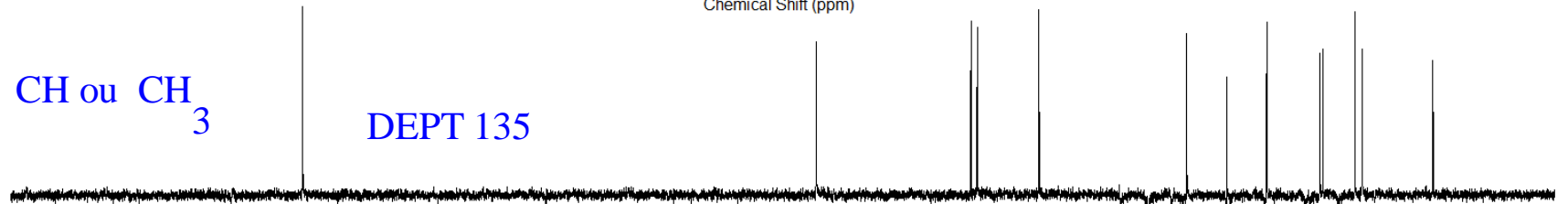
CH

DEPT 90

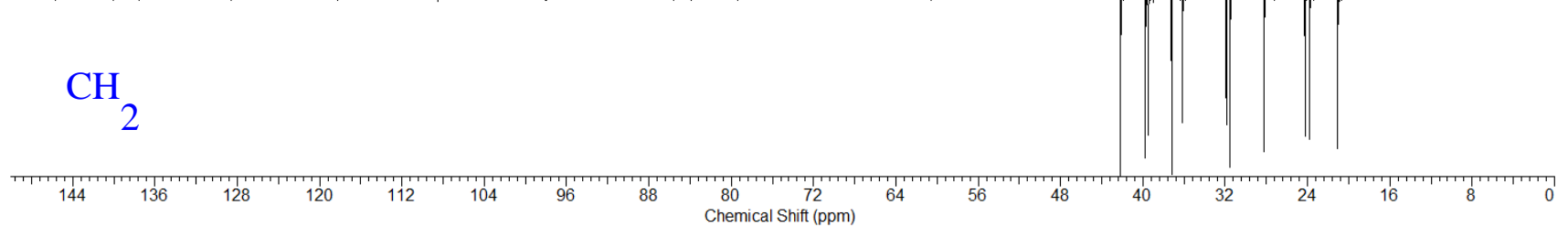


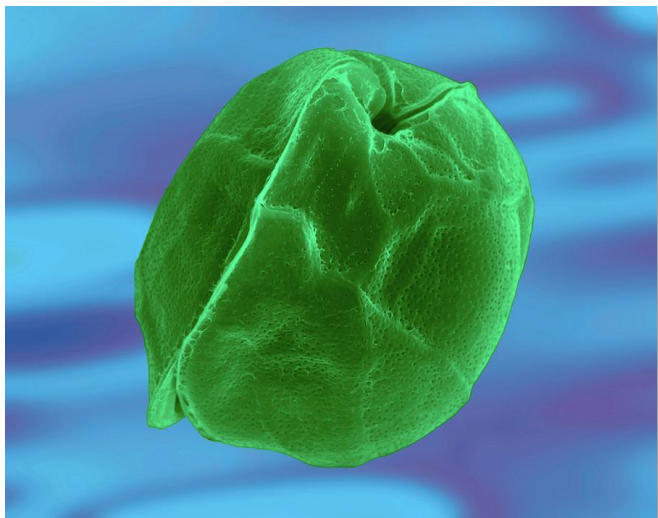
CH ou  $\text{CH}_3$

DEPT 135



$\text{CH}_2$



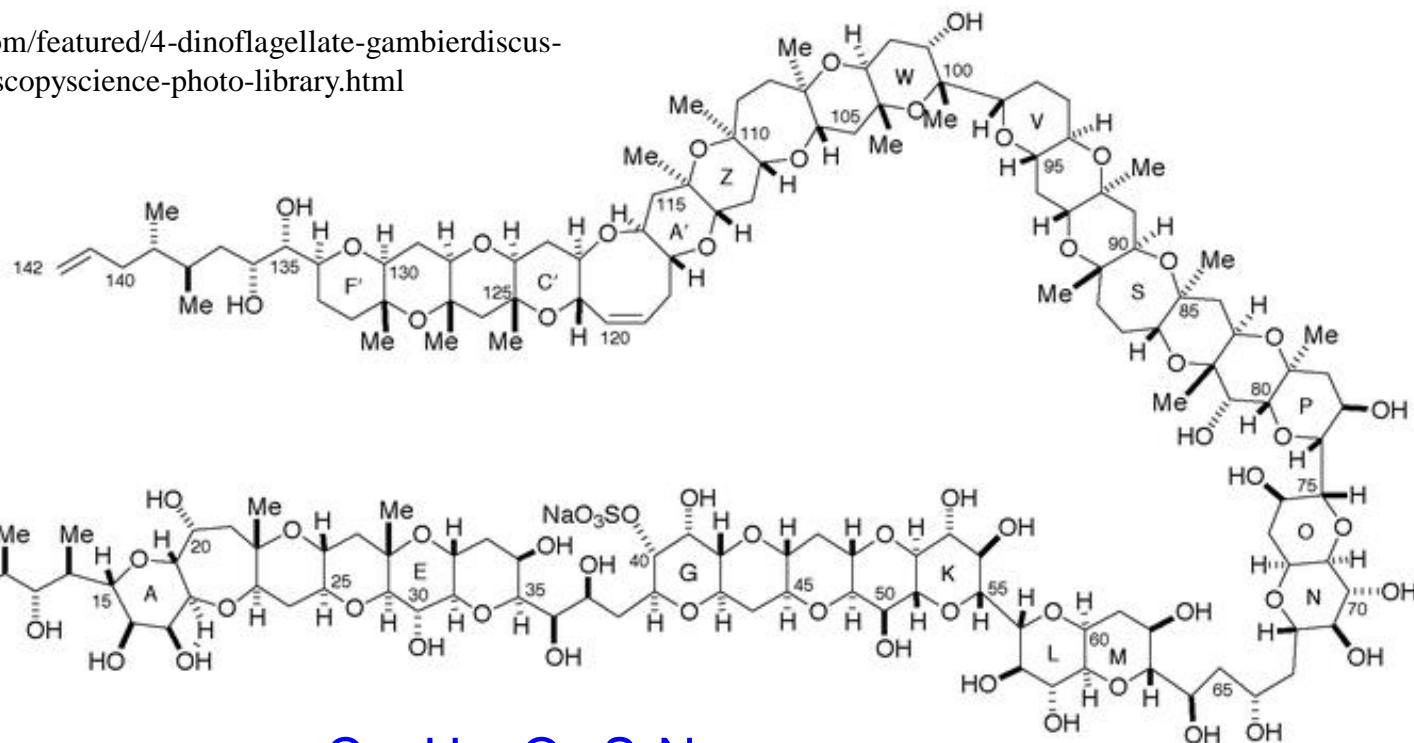


## *Gambierdiscus toxicus* (dinoflagelado)

<https://en.wikipedia.org/wiki/Maitotoxin>

*Gambierdiscus toxicus* foi descoberto em 1975 em material coletado em torno das Ilhas **Gambier**, onde ciguatera ocorre com frequência, e descrito em 1979. Como a maioria dos dinoflagelados, é unicelular e coberto de placas rígidas formando uma estrutura chamada teca.

<https://sciencephotogallery.com/featured/4-dinoflagellate-gambierdiscus-toxicus-dennis-kunkel-microscopyscience-photo-library.html>



maitoxina



Maitotoxin was named from the ciguateric fish *Ctenochaetus striatus*—called "maito" in Tahiti—from which maitotoxin was isolated for the first time

#### Disodium

(12S,14aR,15aS,16aR,17aS,18Z,110aR,111aS,112aR,113aS,114aR,116R,117R,118aS,119aR,121aS,122aR,123aS,124aR,125aS,126aR,127aS,22S,24aR,25aS,26aR,27aS,28aR,29aS,211R,212R,213aR,214S,214aS,215aR,217aS,218aR,219aS,32R,33R,34aS,36S,37R,38R,38aS,5R,7R,82S,83R,84aS,86R,87R,88R,88aS,92R,93R,94R,94aS,95aS,96aR,97aS,98R,99R,910S,911aR,912aS,913aR,914R,914aR,11S,12R,132S,133R,134S,134aS,135aR,136aS,137aR,138S,138aS,1310S,1311R,1312aR,1313aS,1314aR,1315aS,1317R,1317aR)-12-[(1S,2R,4R,5S)-1,2-dihydroxy-4,5-dimethyloct-7-en-1-yl]-117,211,214,33,37,38,5,7,83,87,88,93,94,98,914,11,12,133,134,138,1311,1317-docosahydroxy-14a,15a,16a,114a,116,119a,121a,122a,25a,27a,29a,214a,217a,1313a,1315a-pentadecamethyl-132-[(2R,3R,4R,7S,8R,9R,11R,13E)-3,8,11,15-tetrahydroxy-4,9,13-trimethyl-12-methylidene-7-(sulfonatoxy)pentadec-13-en-2-yl]-13,14,14a,15a,16,16a,17a,110,110a,111a,112,112a,113a,114,114a,116,117,118,118a,119a,120,121,121a,122a,123,123a,124a,125,125a,126a,127,127a,22,23,24,24a,25a,26,26a,27a,28,28a,29a,210,211,212,213a,214,214a,215a,216,217,217a,218a,219,219a,32,33,34,34a,36,37,38,38a,82,83,84,84a,86,87,88,88a,93,94,94a,95a,96,96a,97a,98,99,910,911a,912,912a,913a,914,914a,133,134,134a,135a,136,136a,137a,138,138a,1310,1311,1312,1312a,1313a,1314,1314a,1315a,1316,1317,1317a-octahectahydro-12H,92H,132H-1(16)-pyrano[2'''',3''':5''',6''']pyrano[2''',3''':6'',7'']oxepino[2'',3'':5',6']pyrano[2',3':5,6]pyrano[3,2-b]pyrano[2''',3''':5'',6''']pyrano[2'',3'':5',6']pyrano[2',3':5,6]pyrano[2,3-g]oxocina-2(2,12)-bis(pyrano[2'',3'':5',6']pyrano[2',3':5,6]pyrano)[3,2-b:2',3'-f]oxepina-13(10)-pyrano[3,2-b]pyrano[2''',3''':5'',6''']pyrano[2'',3'':5',6']pyrano[2',3':5,6]pyrano[2,3-f]oxepina-9(2,10)-dipyran[2,3-e:2',3'-e']pyrano[3,2-b:5,6-b']dipyran-3,8(2,6)-bis(pyrano[3,2-b]pyrana)tridecaphan-99-yl sulfate

Maitotoxin is so potent that it has been demonstrated that an intraperitoneal injection of 130 ng/kg was lethal in mice

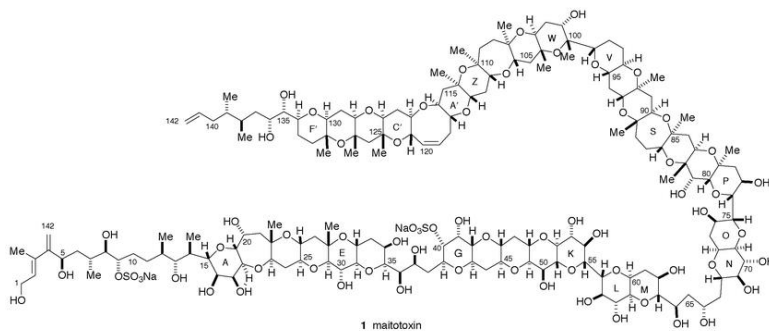
The molecule itself is a system of 32 fused rings. It resembles large fatty acid chains and it is notable because **it is one of the largest and most complex non-protein, non-polysaccharide molecules produced by any organism.**

Maitotoxin includes 32 ether rings, 22 methyl groups, 28 hydroxyl groups, and 2 sulfuric acid esters and has an amphipathic structure. Its structure was established through analysis using **NMR** at Tohoku University, Harvard University and the University of Tokyo in combination with **mass spectrometry**, and **synthetic chemical methods**.

However, Andrew Gallimore and Jonathan Spencer have questioned the structure of maitotoxin at a single ring-junction (the J–K junction), based purely on biosynthetic considerations and their general model for marine polyether biogenesis.

K. C. Nicolaou and Michael Frederick argue that despite this biosynthetic argument, the originally proposed structure could still be correct. The controversy has yet[needs update] to be resolved.

<https://en.wikipedia.org/wiki/Maitotoxin>



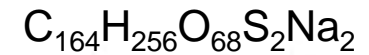
# maitotoxina

*Gambierdiscus toxicus*  
(dinoflagelado)

<https://en.wikipedia.org/wiki/Maitotoxin>

Summary  
of the carbons  
of maitotoxin

	CH <sub>3</sub>	CH <sub>2</sub>	CH	C	
C=C	0	2	4	2	8
C-O	0	1	78	15	94
C-C	21	36	8	0	62
C	21	39	87	17	164
H	63	78	87	0	256 <sup>a</sup>



<sup>a</sup> The number includes the OH protons.

