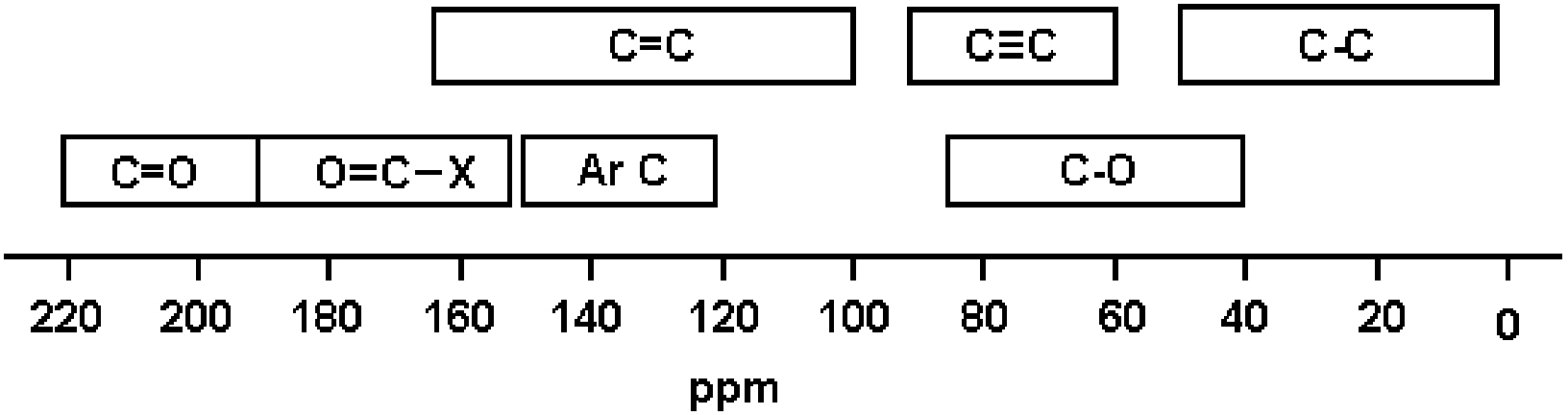
^{13}C-NMR Spectroscopy and Instrumentation

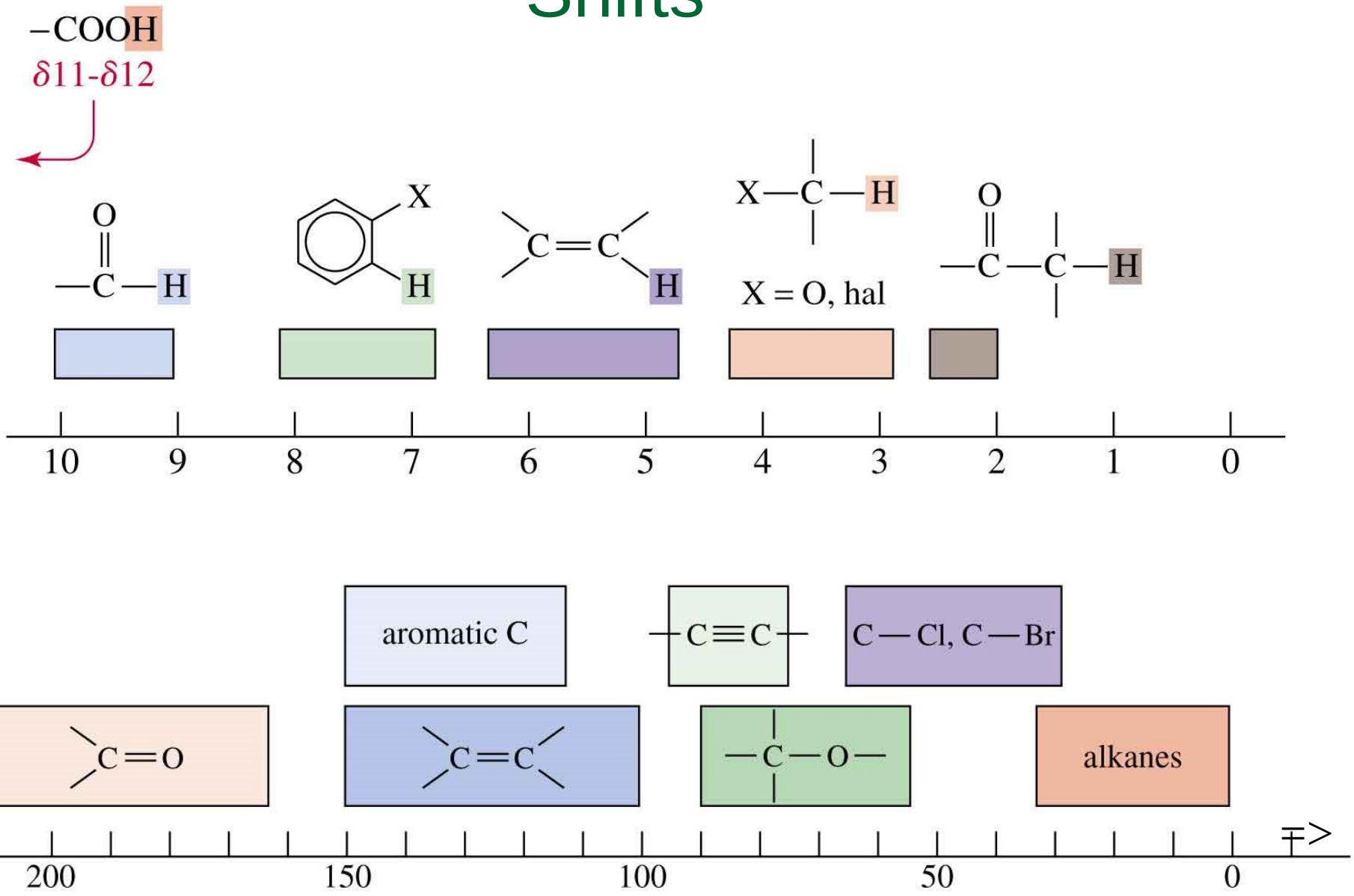
^{13}C-NMR Spectroscopy

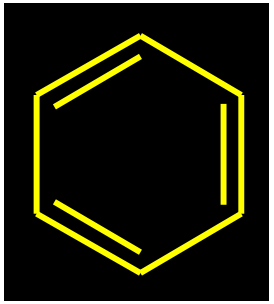
- ^{13}C has only about 1.1% natural abundance (^{13}C resonance is relatively weak).
- C is about 400 times less sensitive than H nucleus to the NMR phenomena
- Chemical shift range is normally 0 to 220 ppm
- Chemical shifts measured with respect to TMS
- We do not usually see ^{13}C-^{13}C coupling
- Similar factors affect the chemical shifts in C^{13} as seen for H NMR
- The peaks show as single lines
- Number of peaks indicates the number of types of C

Carbon NMR



Hydrogen and Carbon Chemical Shifts



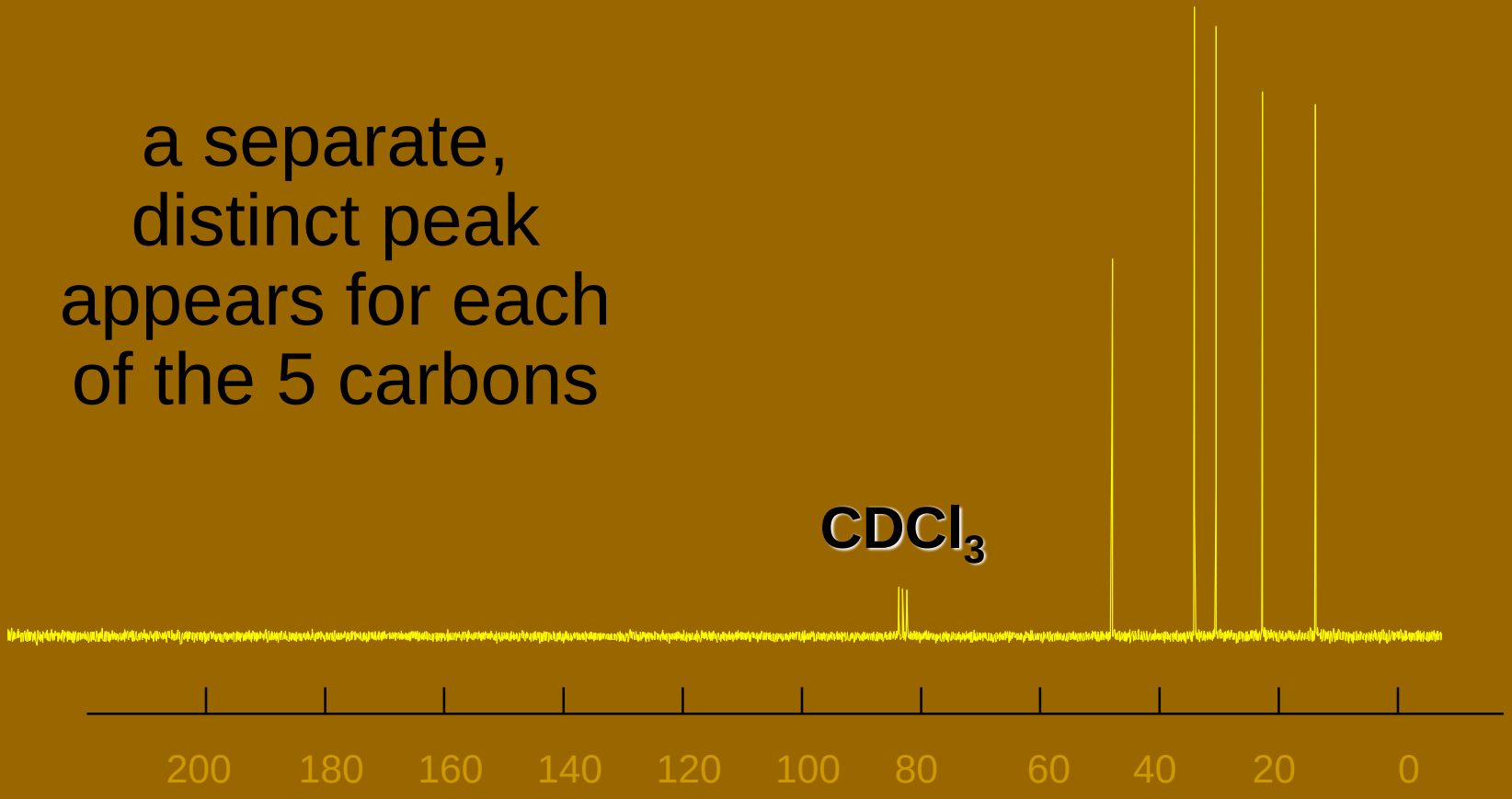
Type of carbon	Chemical shift (δ), ppm	Type of carbon	Chemical shift (δ), ppm
RCH_3	0-35	$RC \equiv CR$	65-90
R_2CH_2	15-40	$R_2C = CR_2$	100-150
R_3CH	25-50		110-175
R_4C	30-40		

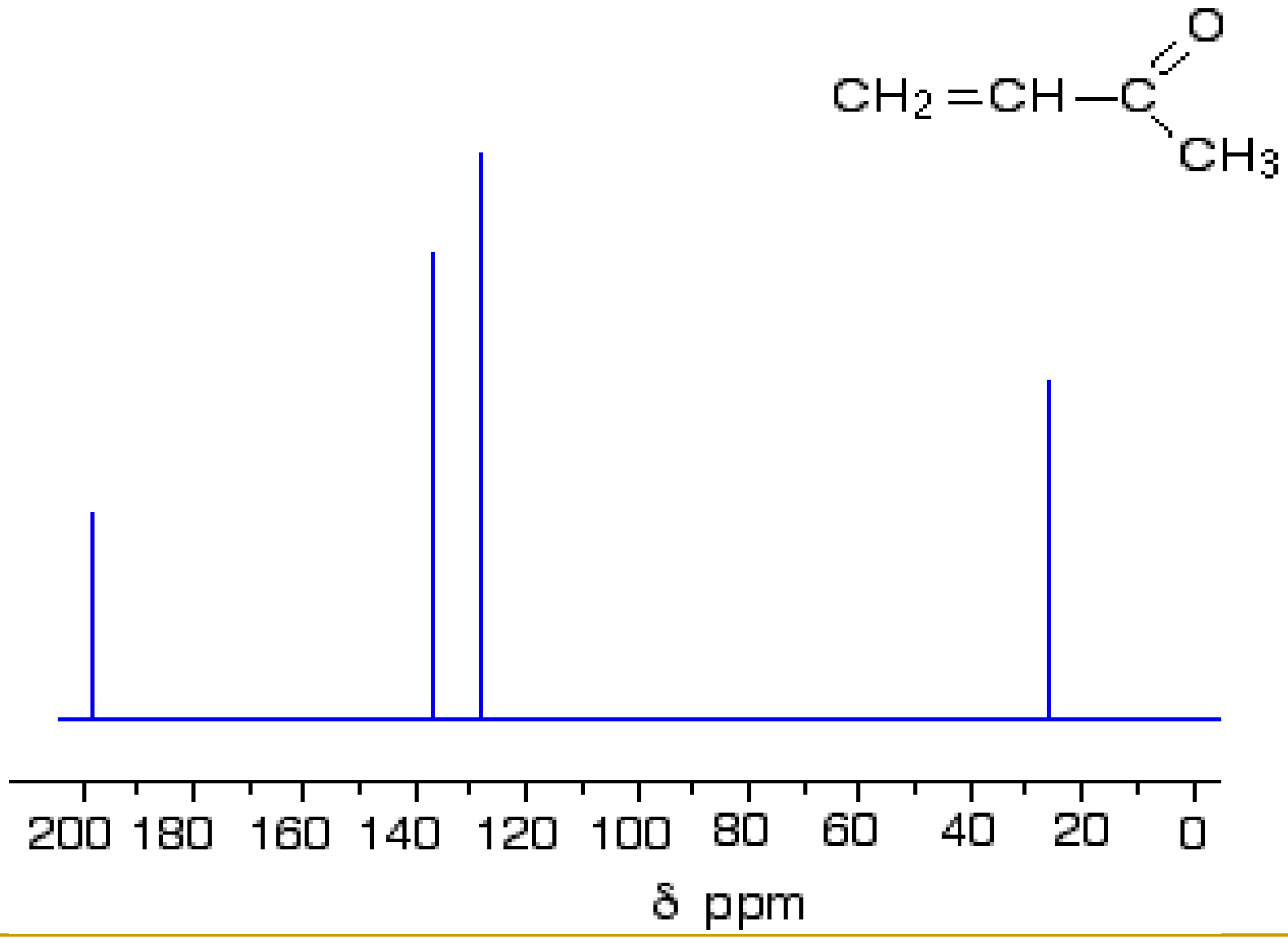
Type of carbon	Chemical shift (δ), ppm	Type of carbon	Chemical shift (δ), ppm
RCH_2Br	20-40		160-185
RCH_2Cl	25-50		
RCH_2NH_2	35-50		190-220
RCH_2OH	50-65		
RCH_2OR	50-65		

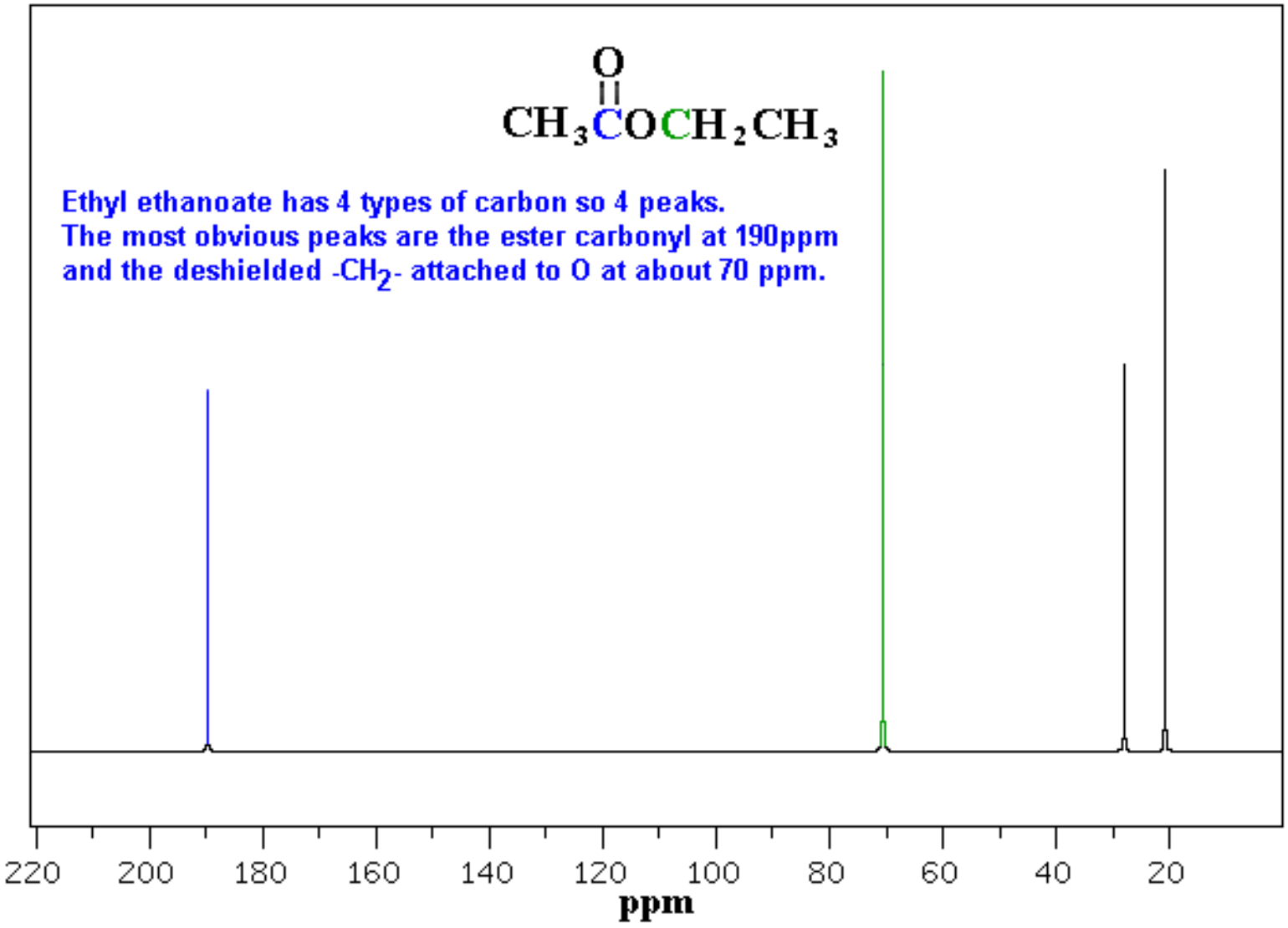
^{13}C

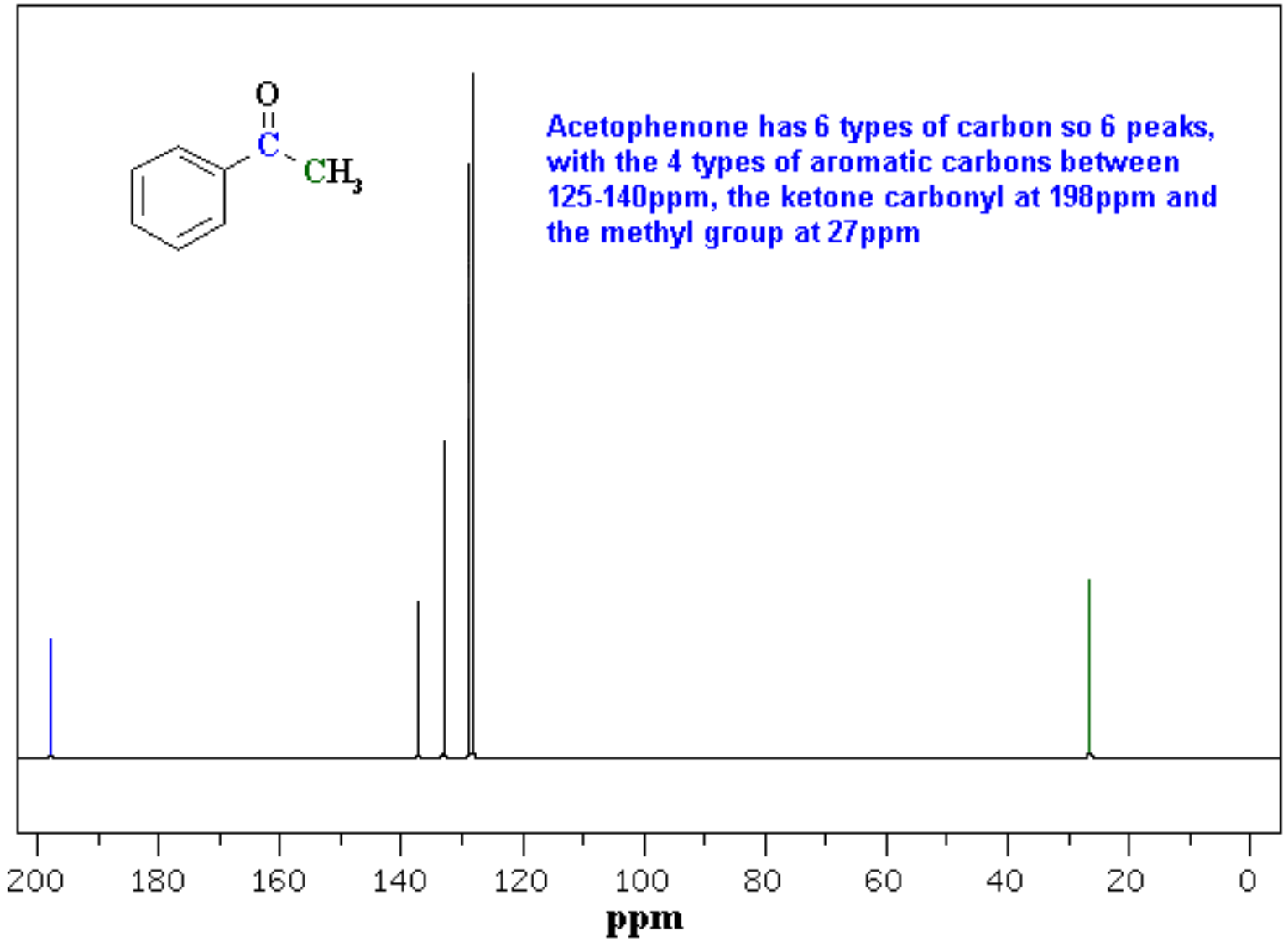
$ClCH_2CH_2CH_2CH_2CH_3$

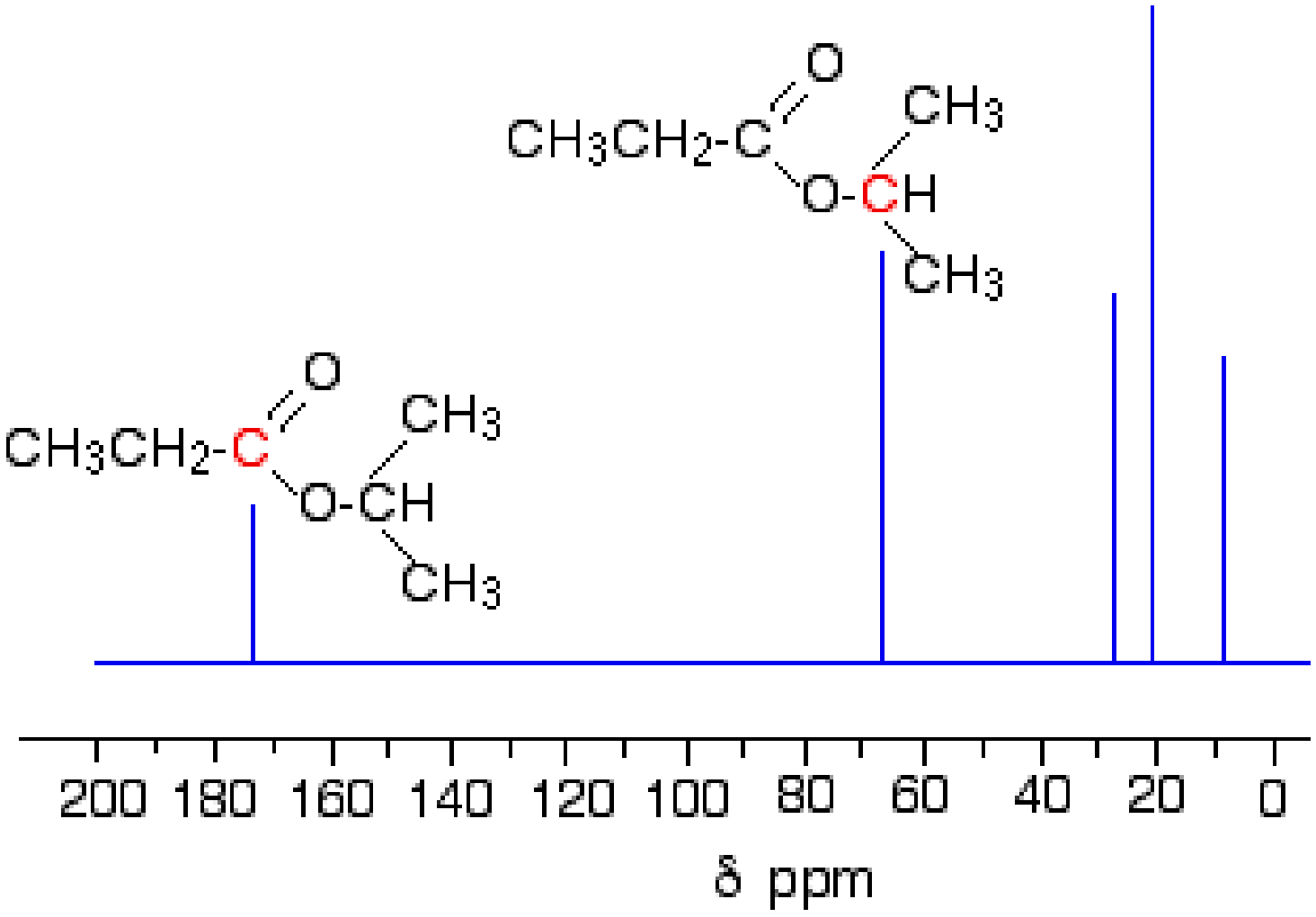
a separate, distinct peak appears for each of the 5 carbons

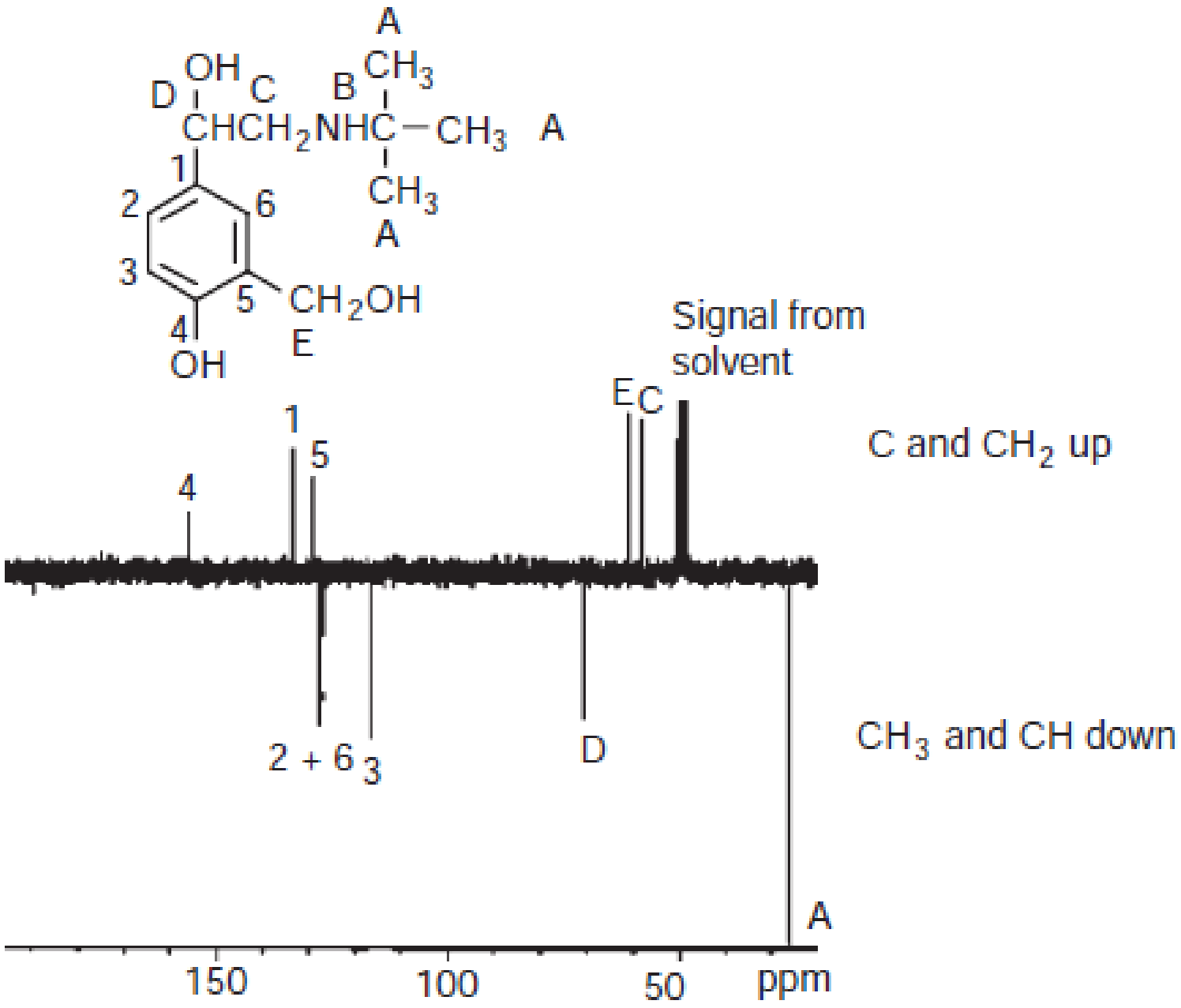



CH2 =CH —C
O
CH3
200 180 160 140 120 100 80 60 40 20 0
δ ppm


O
CH3COCH2CH3
Ethyl ethanoate has 4 types of carbon so 4 peaks.
The most obvious peaks are the ester carbonyl at 190ppm
and the deshielded -CH2- attached to O at about 70 ppm.
220
200
180
160
140
120
100
80
60
40
20
ppm


O
C
CH3
Acetophenone has 6 types of carbon so 6 peaks, with the 4 types of aromatic carbons between 125-140ppm, the ketone carbonyl at 198ppm and the methyl group at 27ppm
200
180
160
140
120
100
80
60
40
20
0
ppm


CH3CH2-C
O
O-CH
CH3
CH3
CH3CH2-C
O
O-CH
CH3
CH3
200 180 160 140 120 100 80 60 40 20 0
δ ppm


A
OH
D
C
B
CH3
CHCH2NHC–CH3
A
1
2
6
CH3
A
3
5
CH2OH
4
E
OH
Signal from solvent
E
C
1
5
4
C and CH2 up
2 + 6
3
D
CH3 and CH down
A
150
100
50
ppm

Solvents for NMR spectroscopy

- NMR spectra are usually measured using solutions of the substance being investigated. A commonly used solvent is $CDCl_3$ This is a trichloromethane (chloroform) molecule in which the hydrogen has been replaced by its isotope, deuterium.

- Examples of NMR lock solvents are;

  Acetone CD_3COCD_3, Chloroform $CDCl_3$. Dichloro Methane CD_2Cl_2, Dimethyl Sulfoxide (DMSO) CD_3SOCD_3, Ethanol CD_3CD_2OD and Methanol CD_3OD

The NMR Spectrometer

Applications in pharmaceutical analysis

- A powerful technique for the characterisation of the exact structure of raw materials, intermediates and finished products.
- Can determine impurities, including enantiomeric impurities, without separation.
- Can potentially be used for fingerprinting mixtures.
- Has good potential for non-destructive quantitative analysis of drugs in formulations without prior separation.

Strengths

- Provides much more information about molecular structure than any other technique
- Results are reproducible between the different instruments available in the market

Limitations

- A relatively insensitive technique for samples <1 mg for proton nuclear magnetic resonance (NMR) and <5 mg for carbon-13 NMR
- Expensive instrumentation requiring a specialist operator, although automation is increasingly available for routine methods.