

To understand NMR you need to know the following:

A. Physics: Moving charge generates a magnetic field, and a moving magnetic field causes charges to move in a conductor.

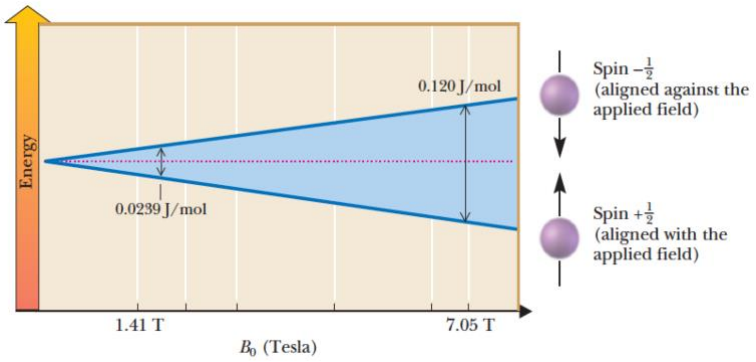
B. Atomic nuclei, like electrons, have a quantum mechanical property of "spin". Spin can be thought of as a small magnetic field around the nucleus created as if the positive charge of the nucleus were circulating.

C. NMR, nuclear magnetic resonance, is used to assign structures of organic molecules.

D. We care about the nuclei ^{1}H and ^{13}C since these are commonly found in organic molecules and they have spin quantum numbers of 1/2.

E. Nuclei with spin quantum number 1/2 are quantized in one of two orientations, "+1/2" (lower energy) or "-1/2"(higher energy) in the presence of an external magnetic field, that is, with and against the external field, respectively.

F. **The difference in energy between the +1/2 and -1/2 nuclear spin states is proportional to the strength of the magnetic field felt by the nucleus.**

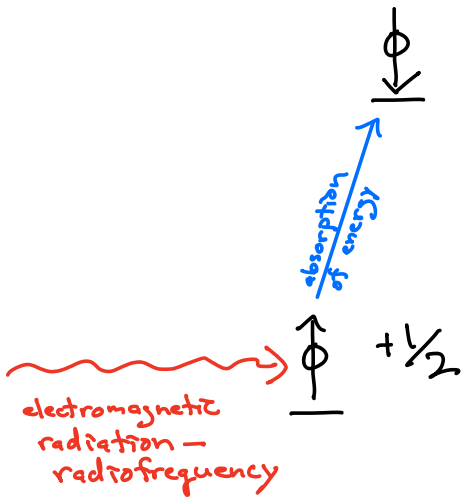


G. Electron density is induced to circulate in a strong external magnetic field, which in turn produces a magnetic field that opposes the external magnetic field. This **shields** nuclei from the external magnetic field. The greater the electron density around a nucleus, the more shielded it is, and the lower the energy (frequency) of electromagnetic radiation required to flip its nuclear spin.

H. In the classic ^{1}H-NMR experiment, the molecule of interest is placed in solvent (the solvent has deuterium atoms in place of H atoms so the solvent molecules will not show up in the spectra, see R.) then is put in a spinning tube in a very strong magnetic field. The sample is exposed to radiofrequency irradiation and if it is of exactly the right frequency energy is absorbed and spins flip from +1/2 to -1/2 (come into resonance). The absorbed energy is plotted in the spectra.

I. All ^{1}H-NMR spectra are recorded as **chemical shift (∂, delta)** in the units of **ppm** (parts per million). Shielding magnetic field effects are around 1 millionth as large as the external magnetic field in which the sample is placed. Tetramethylsilane (TMS, $(CH_3)_4Si$)) is placed in the sample as a standard and assigned the value of 0.0 ppm. ***Warning the NMR scale is plotted "backwards", with higher values to the left!!***

NMR experiment → place sample of a molecule in a very strong magnetic field

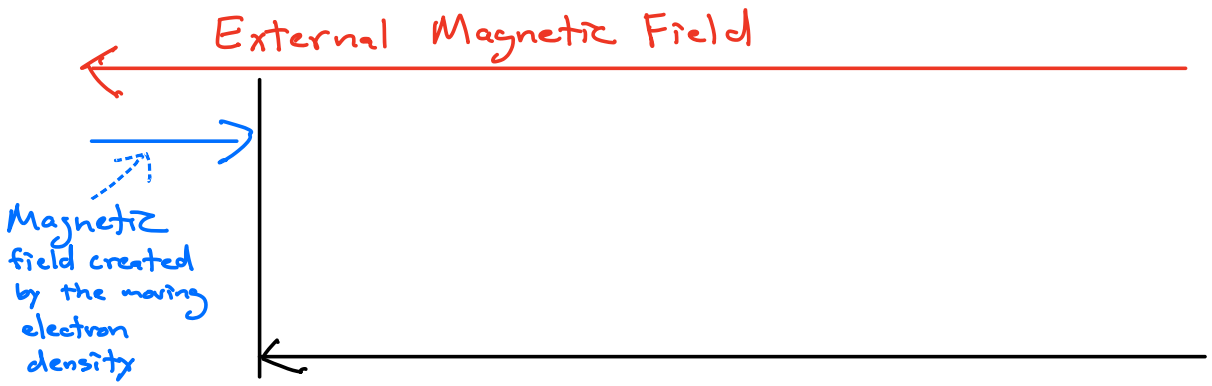


The energy absorption/nuclear spin flipping phenomenon is called "Resonance"

The ^1H nucleus of spin state $+\frac{1}{2}$ absorbs a quanta of energy of precisely the correct frequency and the nucleus is "excited" to the $-\frac{1}{2}$ spin state

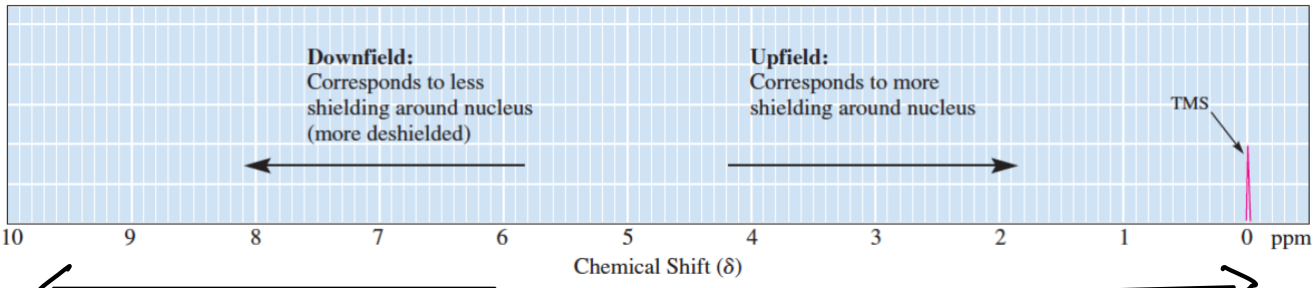
Shielding → explanation

The external magnetic field induces electron density to circulate, which creates its own small magnetic field that will always directly oppose the external magnetic field.



The magnitude of the magnetic field experienced by a nucleus under the electron density.

Plot is backwards → larger values to the LEFT!



Deshielding

Less electron density

Larger difference in energy between +½ and -½ nuclear spin state

Shielding

More electron density

Smaller difference in energy between +½ and -½ nuclear spin state

J. The hybridization state of carbon atoms attached to an H atom influences shielding in predictable ways by removing differing amounts of electron density around adjacent nuclei.

K. Electron density in pi bonds also has a large effect on H atom shielding because pi electrons are more free to circulate in an a magnetic field compared to electron density in sigma bonds. Geometry of the pi bond is important.

Table 13.3 The Effect of Hybridization on Chemical Shift

Type of Hydrogen (R = alkyl)	Name of Hydrogen	Chemical Shift δ
RCH_3, R_2CH_2, R_3CH	Alkyl	0.8–1.7
$R_2C{=}C(R)CHR_2$	Allylic	1.6–2.6
$RC{\equiv}CH$	Acetylenic	2.0–3.0
$R_2C{=}CHR$, $R_2C{=}CH_2$	Vinylic	4.6–5.7
RCHO	Aldehydic	9.5–10.1

Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*	Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*
		RCH_2OH	3.4-4.0
R_2NH	0.5-5.0	RCH_2Br	3.4-3.6
ROH	0.5-6.0	RCH_2Cl	3.6-3.8
RCH_3	0.8-1.0	$RCOCH_3$	3.7-3.9
RCH_2R	1.2-1.4	$RCOCH_2R$	4.1-4.7
R_3CH	1.4-1.7	RCH_2F	4.4-4.5
$R_2C{=}CRCHR_2$	1.6-2.6	$ArOH$	4.5-4.7
$RC{\equiv}CH$	2.0-3.0	$R_2C{=}CH_2$	4.6-5.0
$RCCH_3$	2.1-2.3	$R_2C{=}CHR$	5.0-5.7
$RCCH_2R$	2.2-2.6	$H_2C{-}CH_2$	3.3-4.0
$ArCH_3$	2.2-2.5	RCH	9.5-10.1
RCH_2NR_2	2.3-2.8	$RCOH$	10-13
RCH_2I	3.1-3.3		
RCH_2OR	3.3-4.0		

* Values are relative to tetramethylsilane. Other atoms within the molecule may cause the signal to appear outside these ranges.

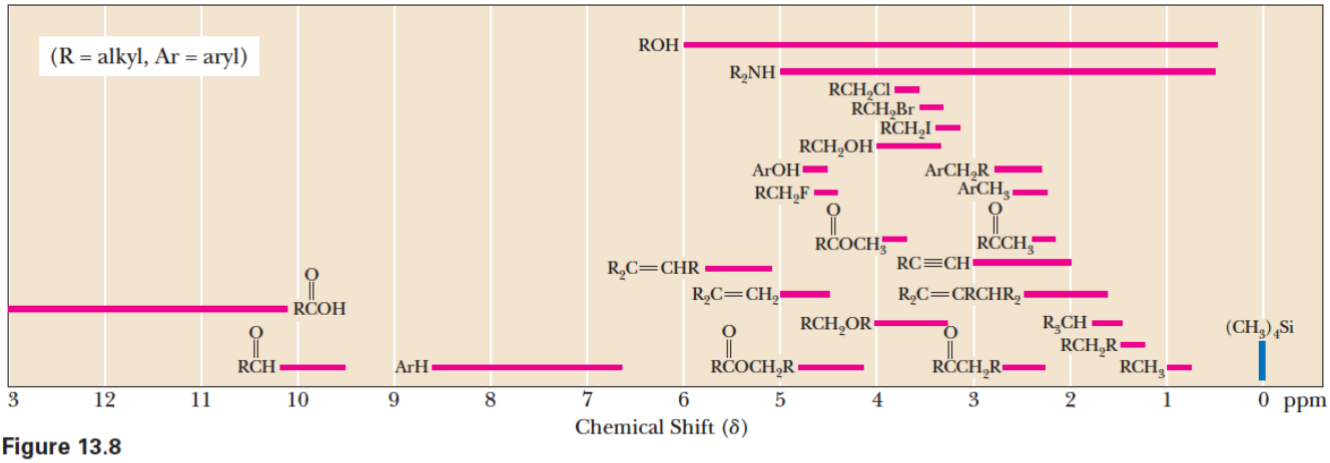
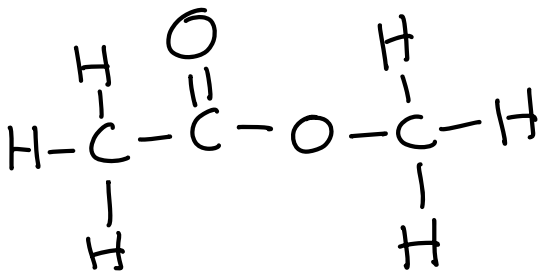


Figure 13.8
Average values of chemical shifts of representative types of hydrogens. These values are approximate. Other atoms or groups in the molecules may cause signals to appear outside of these ranges.

L. Chemically **equivalent** H atoms give rise to the same ^{1}H-NMR signal. **Equivalent** H atoms have the same chemical environment because they are bonded to the same freely rotating sp^3 C atom (molecular motion, nanosecond, is fast compared the time it takes for a spin to flip, microsecond) OR they are equivalent due to symmetry in the molecule.



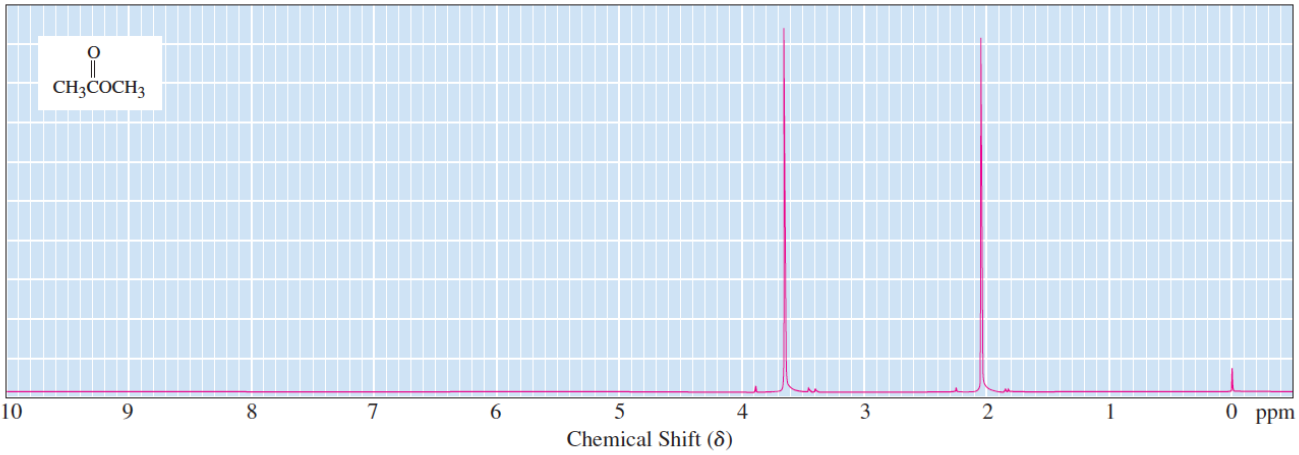


Figure 13.5
^{1}H-NMR spectrum of methyl acetate

M. The area of a ^{1}H-NMR signal is proportional to the number of equivalent H atoms that give rise to that signal.

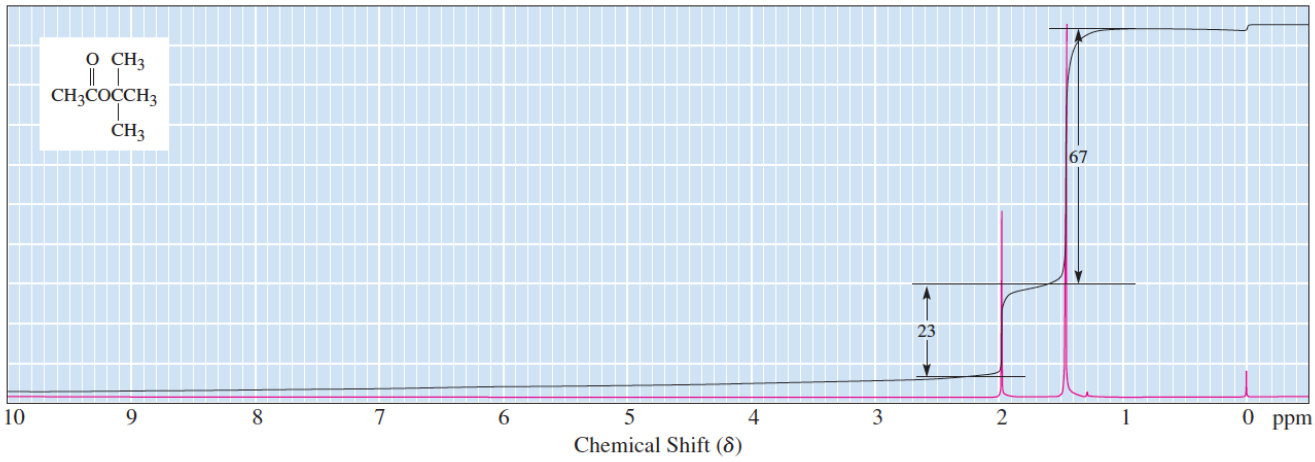
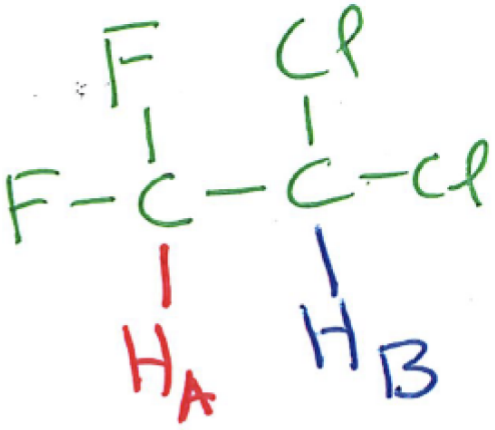


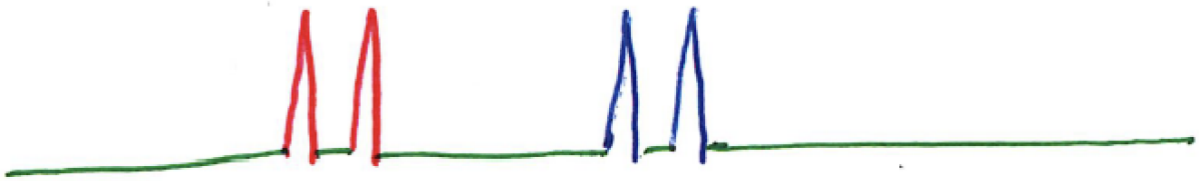
Figure 13.7
^{1}H-NMR spectrum of *tert*-butyl acetate showing the integration. The total vertical rise of 90 chart divisions corresponds to 12 hydrogens, 9 in one set and 3 in the other.

Surprising Fact → The absolute energy difference between ^1H nuclei in a $+1/2$ and $-1/2$ spin state is so small → according to the Boltzmann distribution, at any one time there is only a small excess of ^1H nuclear spins in the $+1/2$ spin state

Definition →

N. Adjacent nuclei have magnetic fields associated with their spins. The spins of equivalent adjacent nuclei can be either +1/2 or -1/2, and at room temperature they are found in about a 50:50 mixture at any given nucleus (very slight excess of lower energy +1/2). These can add to give n+1 different spin **combinations** in the proportions predicted by Pascal's triangle. Each different spin combination produces a different magnetic field, which leads to n+1 splittings in the peaks of the NMR spectra of the adjacent (no more than three bonds away) nuclei.





General case → For "n" equivalent adjacent H atoms a signal is split into "n+1" peaks

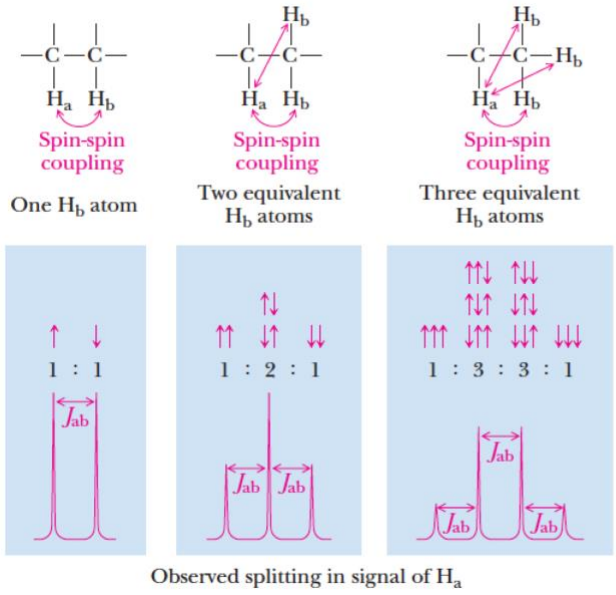


Figure 13.15
The origins of signal splitting patterns. Each arrow represents an H_b nuclear spin orientation.

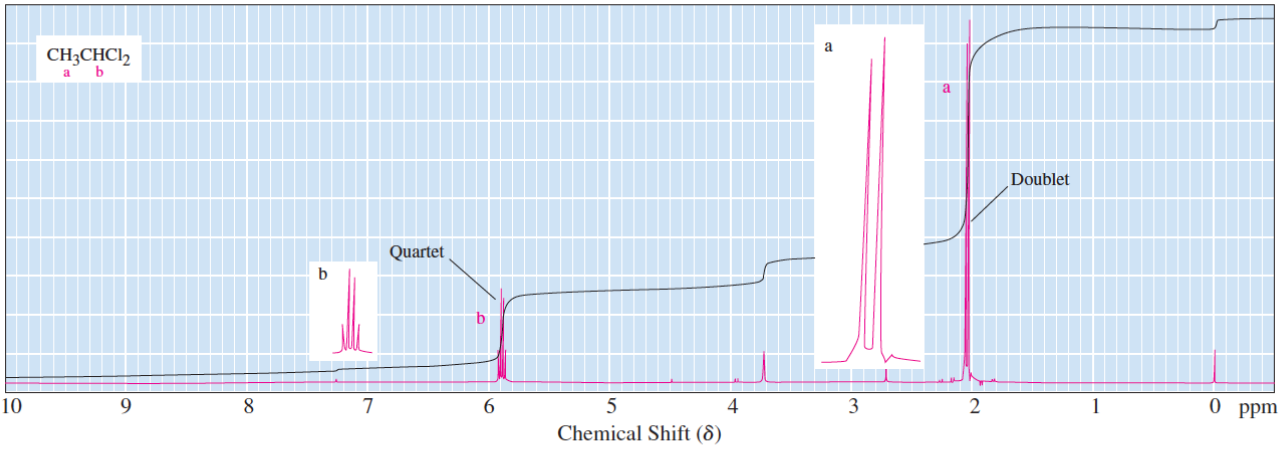
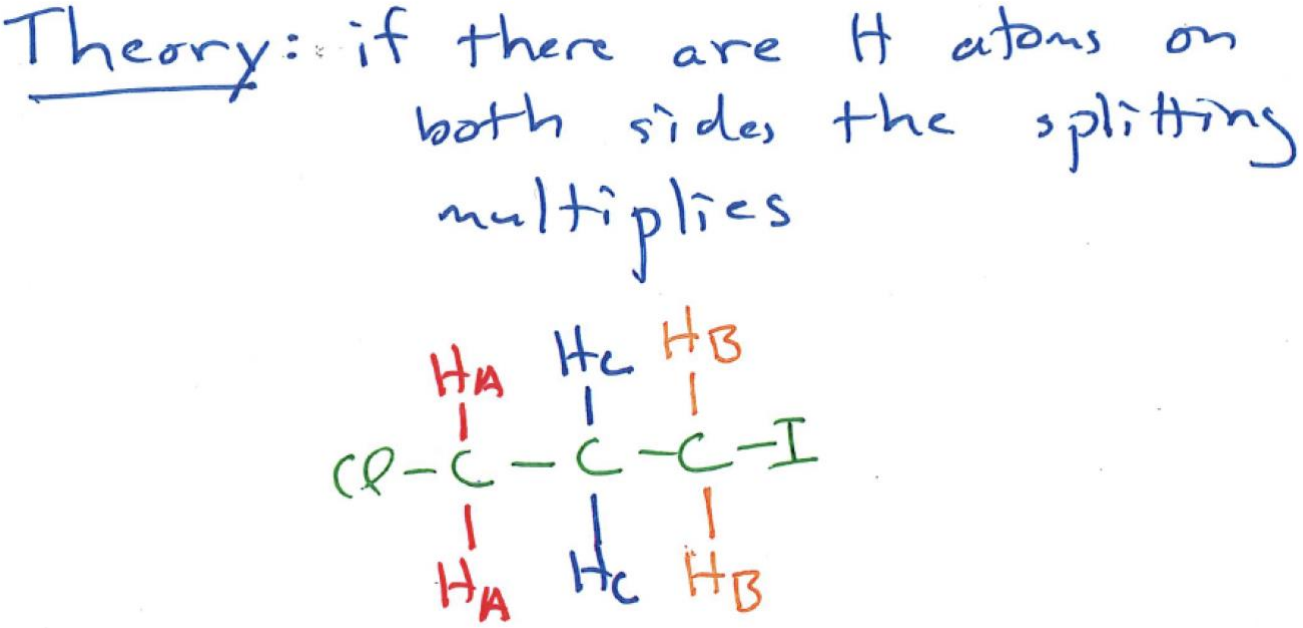
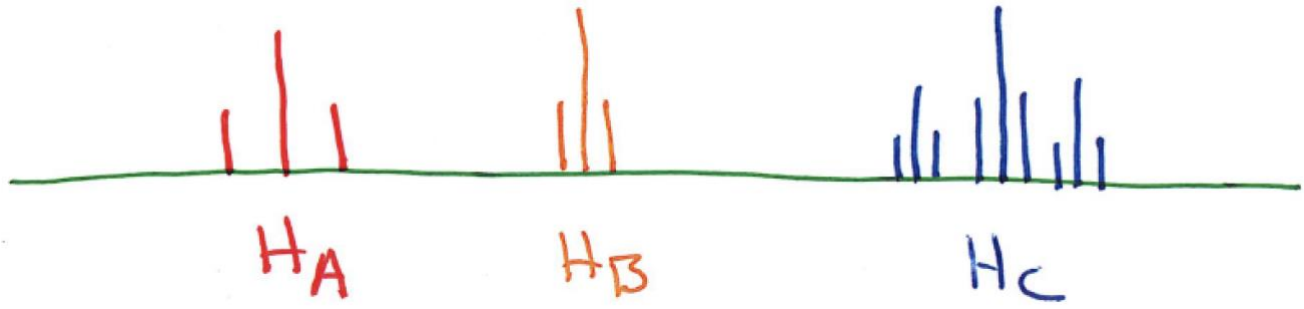


Figure 13.12
^{1}H-NMR spectrum of 1,1-dichloroethane.

O. THEORY: When there are two sets of adjacent H atoms, the number of peaks multiply. For example, a CH_2 group with a CH_2 group and a CH_3group on either side should show 3 x 4 = 12 splittings! You can say this group is a "triplet of quartets" (or a "quartet of triplets").

P. WHAT YOU WILL SEE IN REALITY : For alkyl groups complex splittings simplify because coupling constants ("J") are all about the same. In practice, if there are n adjacent H atoms, equivalent or not, you will see n+1 peaks. This is an approximation, but almost always true on spectra taken with all but the most sophisticated NMR spectrometers.

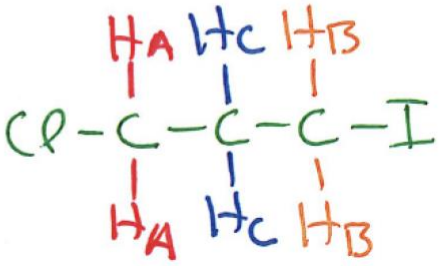


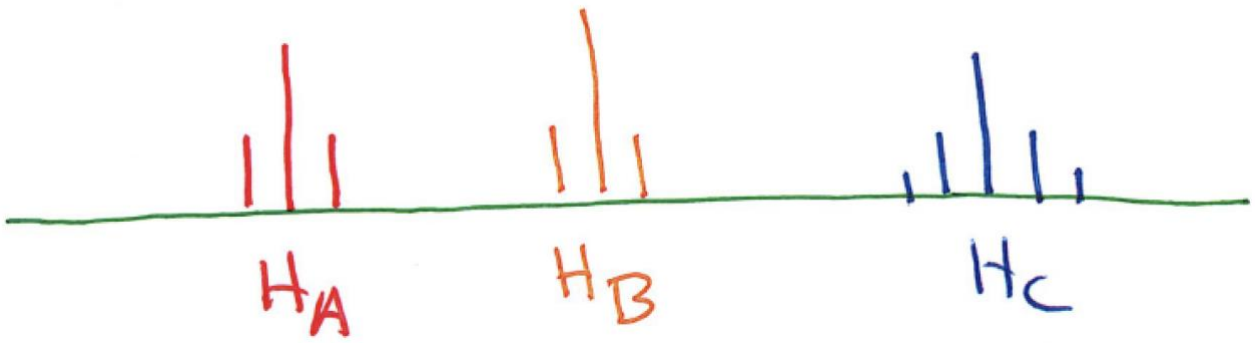


Reality: The splitting does multiply, but $J_{AC} = J_{BC}$ causing overlap of peaks

$\Rightarrow$ we observe $n+1$ peaks

(n = total # of adjacent H atoms)





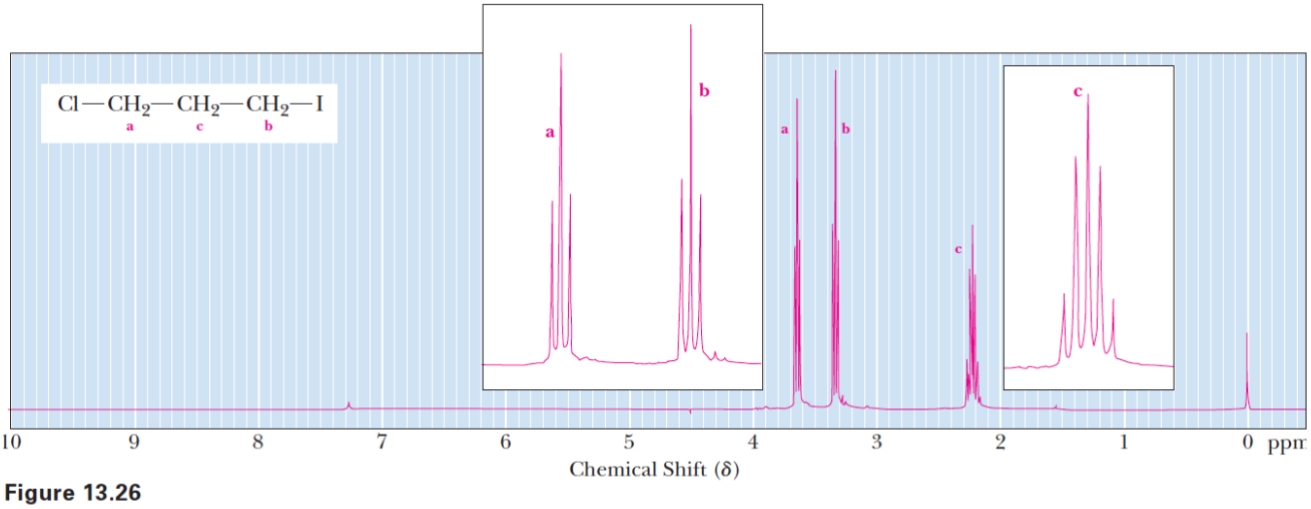


Figure 13.26
300 MHz ^{1}H-NMR spectrum of 1-chloro-3-iodopropane

Recap:

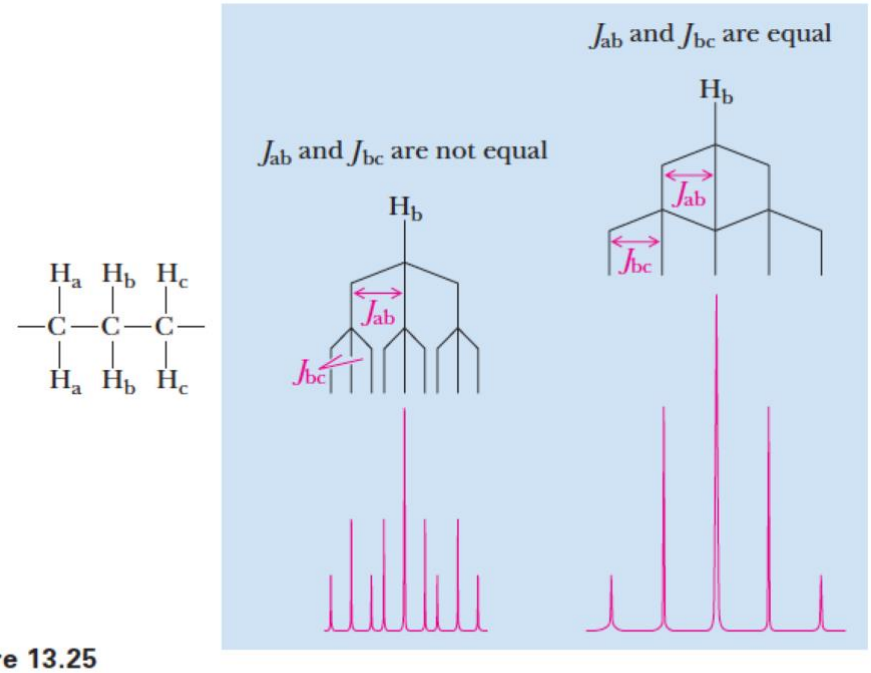


Figure 13.25
Simplification of signal splitting that occurs when coupling constants are the same.

Q. Non-equivalent H atoms on the same C atom can split each other (called geminal coupling), for example on alkenes or small rings. This coupling usually has very small coupling constants, so is difficult to see on some spectra.

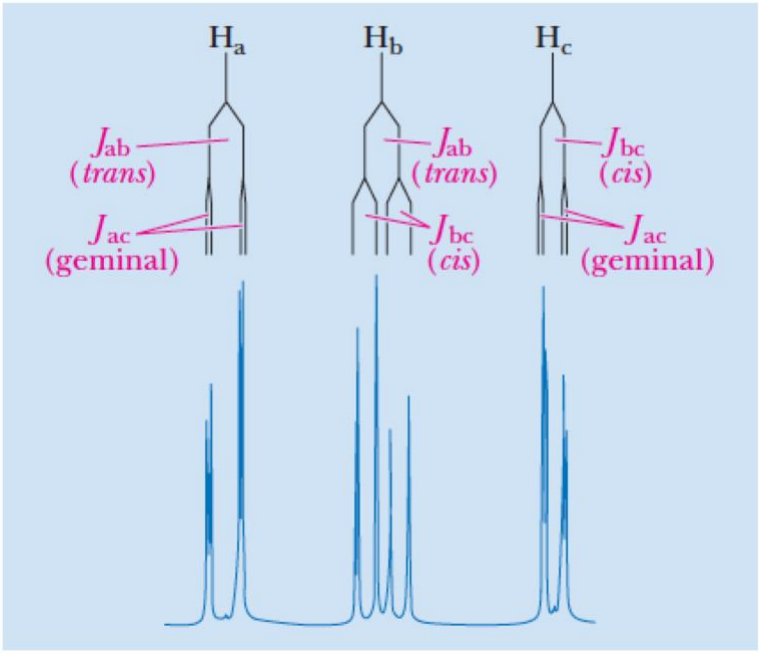


Figure 13.22
Tree diagrams for the complex coupling seen for the alkenyl H atoms in the ^{1}H-NMR spectrum of ethyl propenoate.

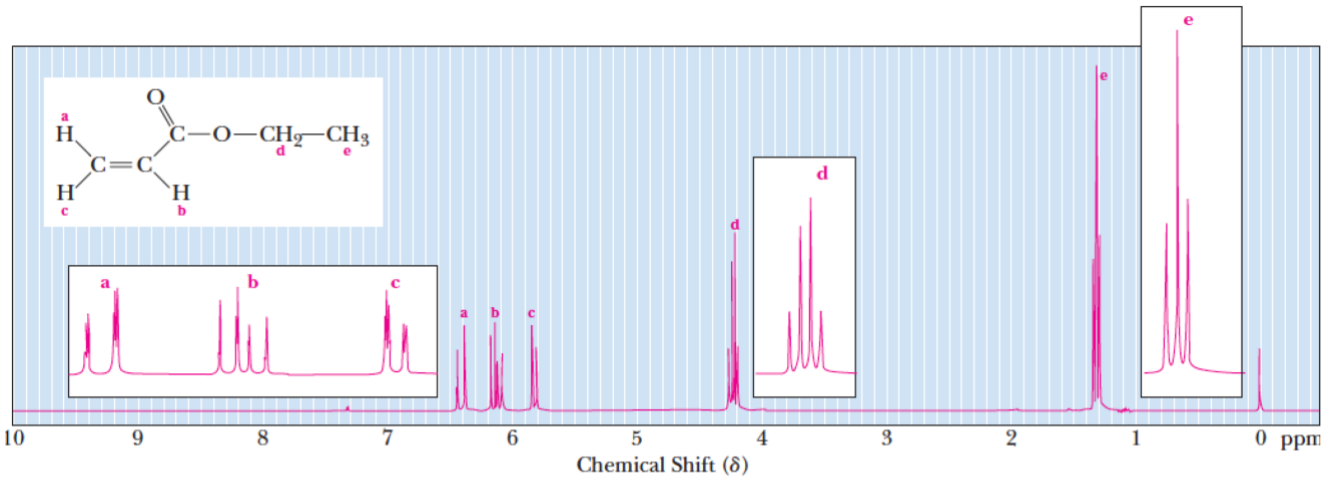
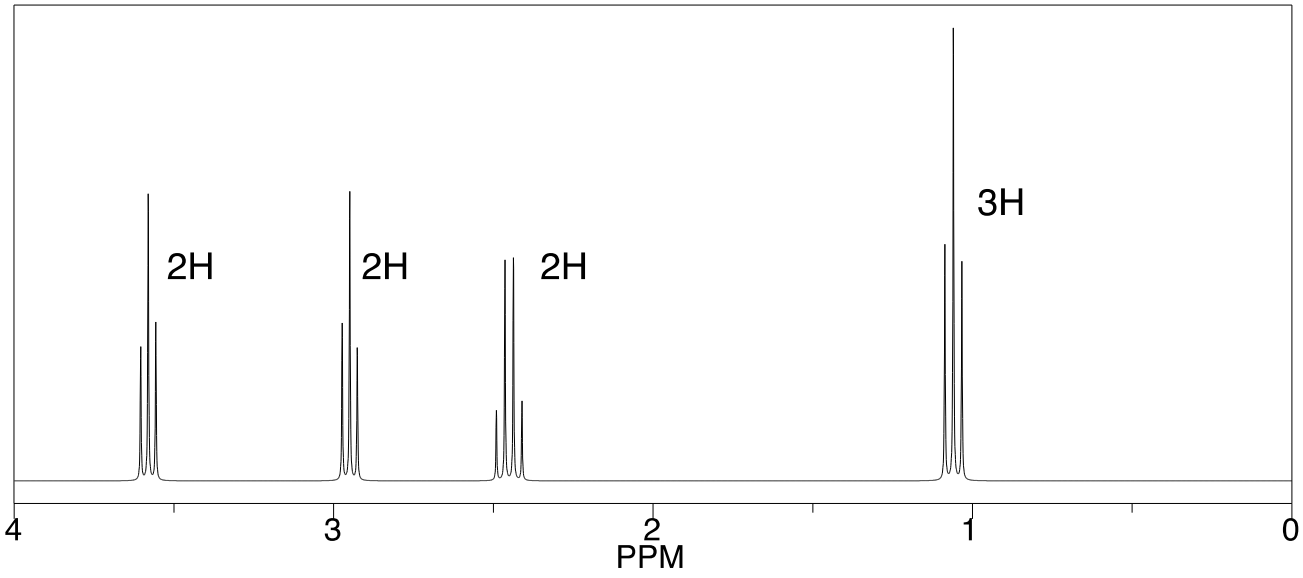
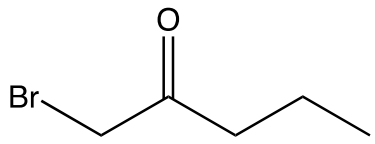


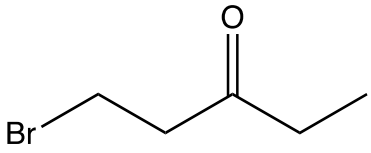
Figure 13.21
300 MHz ^{1}H-NMR spectrum of ethyl propenoate.

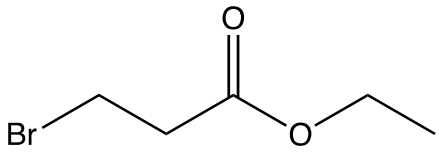
V. When solving NMR spectra problems:

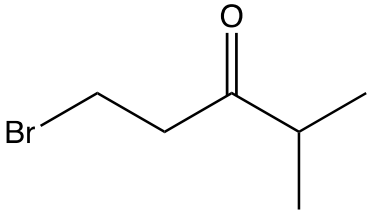
1) **Determine number and relative integrations of signals predicted for a given structure**
2) **Make sure the splitting pattern matches with the spectrum for each signal and**
3) **If the number and relative integrations as well as splitting patterns match with the spectra, compare expected chemical shifts with those of the signals in the spectra.**

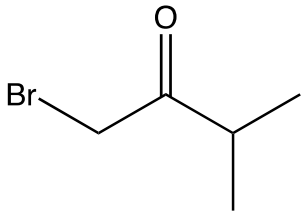


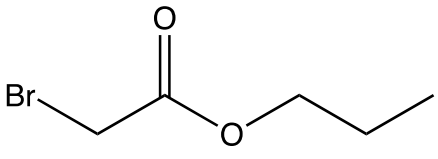






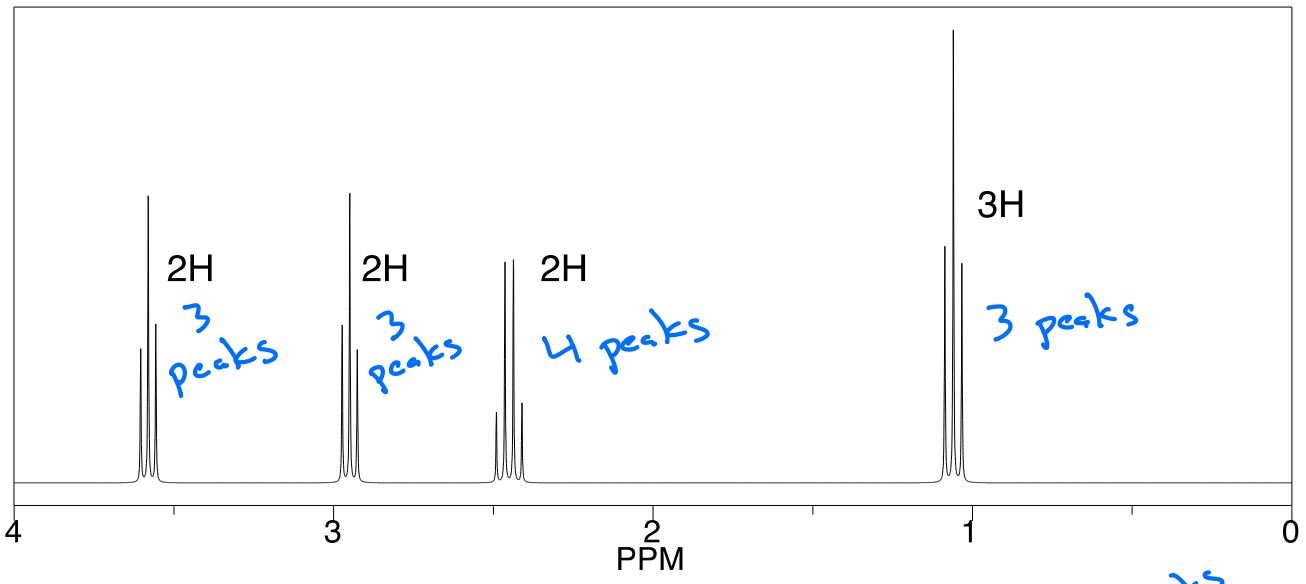


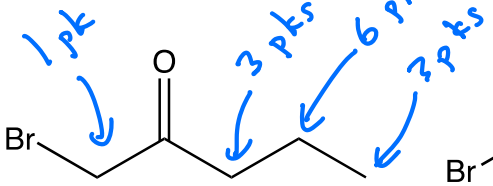




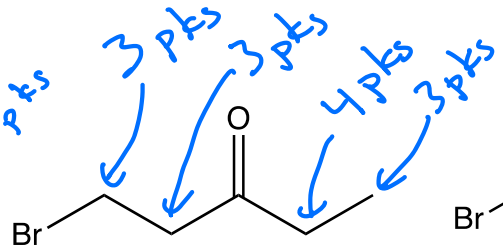
V. When solving NMR spectra problems:

1) **Determine number and relative integrations of signals predicted for a given structure**
2) **Make sure the splitting pattern matches with the spectrum for each signal and**
3) **If the number and relative integrations as well as splitting patterns match with the spectra, compare expected chemical shifts with those of the signals in the spectra.**

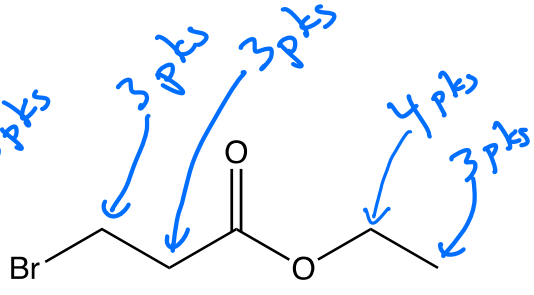




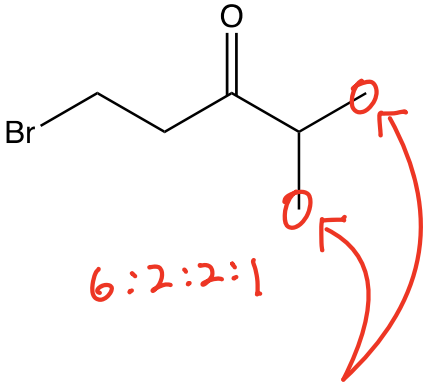
3 : 2 : 2 : 2



3 : 2 : 2 : 2

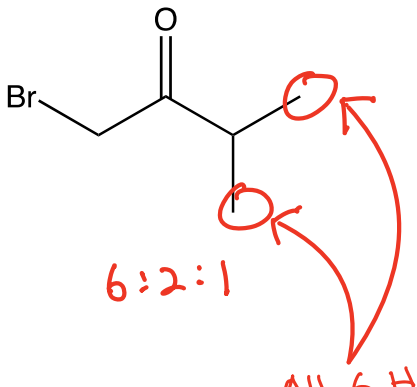


3 : 2 : 2 : 2



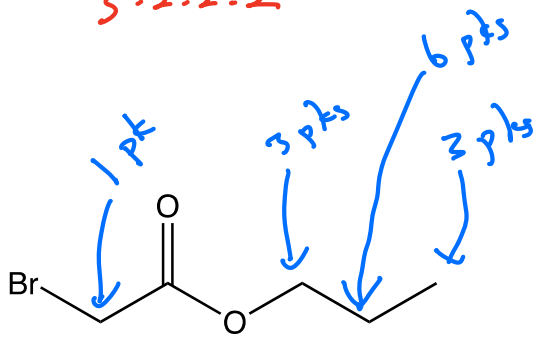
6 : 2 : 2 : 1

All 6 H atoms on the 2 methyl groups are equivalent due to symmetry



6 : 2 : 1

All 6 H atoms on the 2 methyl groups are equivalent due to symmetry



3 : 2 : 2 : 2

Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*	Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*
		RCH_2OH	3.4-4.0
R_2NH	0.5-5.0	RCH_2Br	3.4-3.6
ROH	0.5-6.0	RCH_2Cl	3.6-3.8
RCH_3	0.8-1.0	$RCOCH_3$	3.7-3.9
RCH_2R	1.2-1.4	$RCOCH_2R$	4.1-4.7
R_3CH	1.4-1.7	RCH_2F	4.4-4.5
$R_2C{=}CRCHR_2$	1.6-2.6	$ArOH$	4.5-4.7
$RC{\equiv}CH$	2.0-3.0	$R_2C{=}CH_2$	4.6-5.0
$RCCH_3$	2.1-2.3	$R_2C{=}CHR$	5.0-5.7
$RCCH_2R$	2.2-2.6	$H_2C{-}CH_2$	3.3-4.0
$ArCH_3$	2.2-2.5	RCH	9.5-10.1
RCH_2NR_2	2.3-2.8	$RCOH$	10-13
RCH_2I	3.1-3.3		
RCH_2OR	3.3-4.0		

* Values are relative to tetramethylsilane. Other atoms within the molecule may cause the signal to appear outside these ranges.

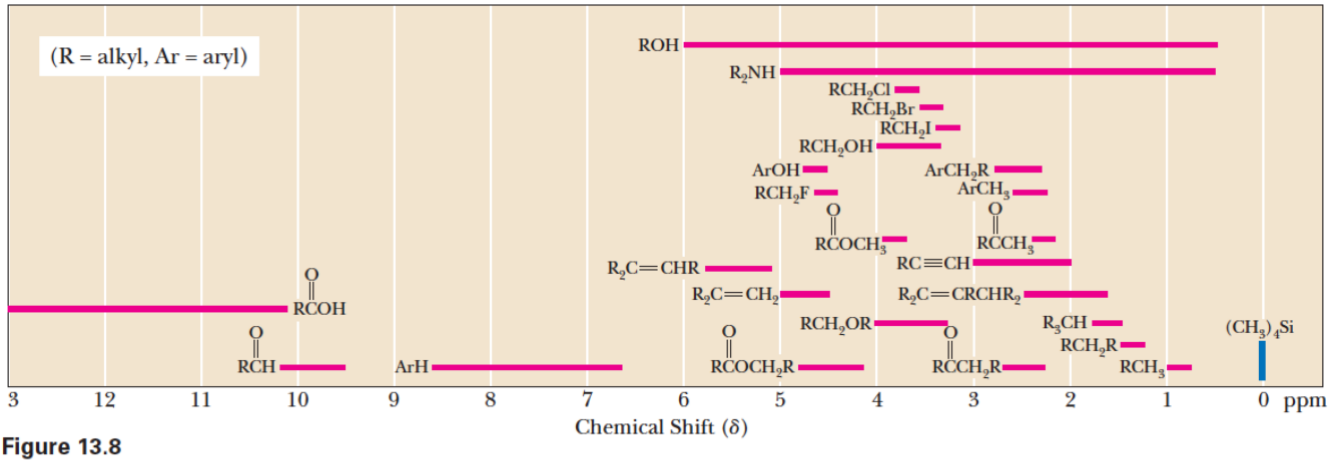


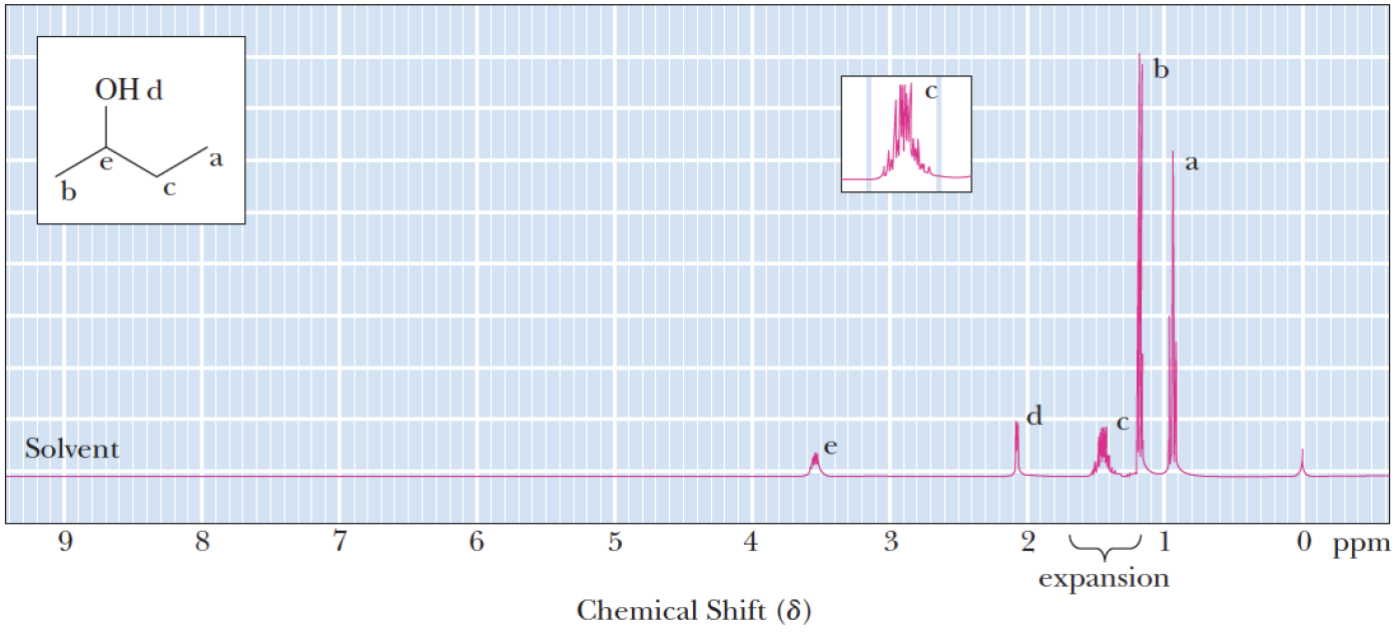
Figure 13.8
Average values of chemical shifts of representative types of hydrogens. These values are approximate. Other atoms or groups in the molecules may cause signals to appear outside of these ranges.

R. Deuterium atoms do not show up in ^{1}H-NMR spectra, so deuerated solvents are used to dissolve NMR samples.

S. The H atoms of relatively acidic functional groups (alcohols, carboxylic acids, amines) exchange rapidly, so they often do not split adjacent protons, and they can be replaced (signal disappears) with deuterium by adding a drop of D_2O to the NMR sample.

T. H-bonding changes the location of a signal for H-bonding groups in a concentration dependent manner explaining why -OH and -NH_2 group signals can vary so much in location.

U. The splitting of a -CH_2- group adjacent to a chiral center will be "messed up", that is split into many peaks. This is useful for identifying chiral centers in molecules.



W. The old way to carry out an NMR experiment: Scan wavelengths (ex. High to low ppm) of radiofrequency electromagnetic radiation then measure absorbance during the scan. This is NOT used any more.

X. What we did not tell you: After a nuclear spin is flipped back from +1/2 to -1/2, it will relax back to the +1/2 spin state and EMIT a photon of the same wavelength it absorbed in the first place.

Y. How modern NMR works:

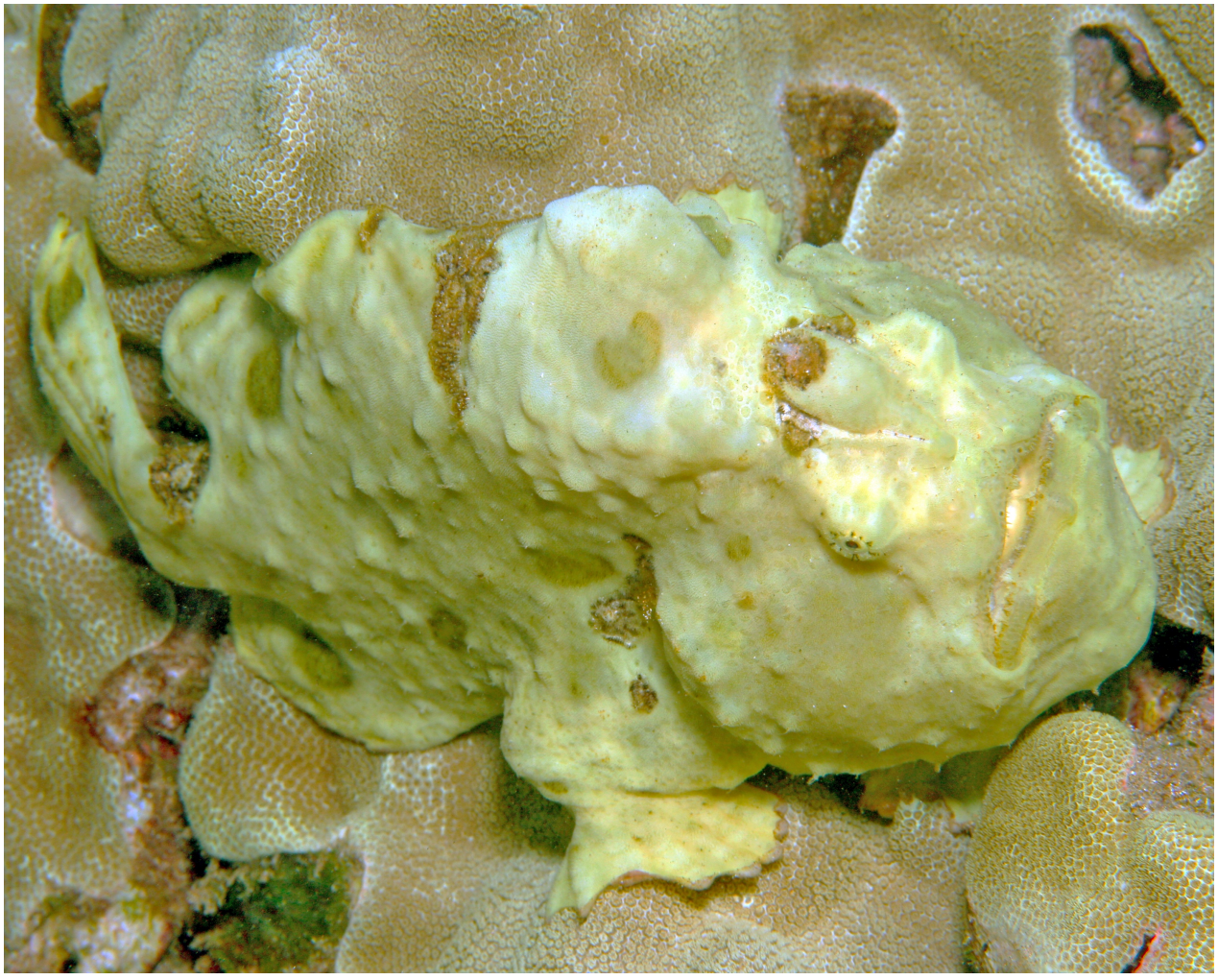
The sample is irradiated with simultaneously in a short blast →

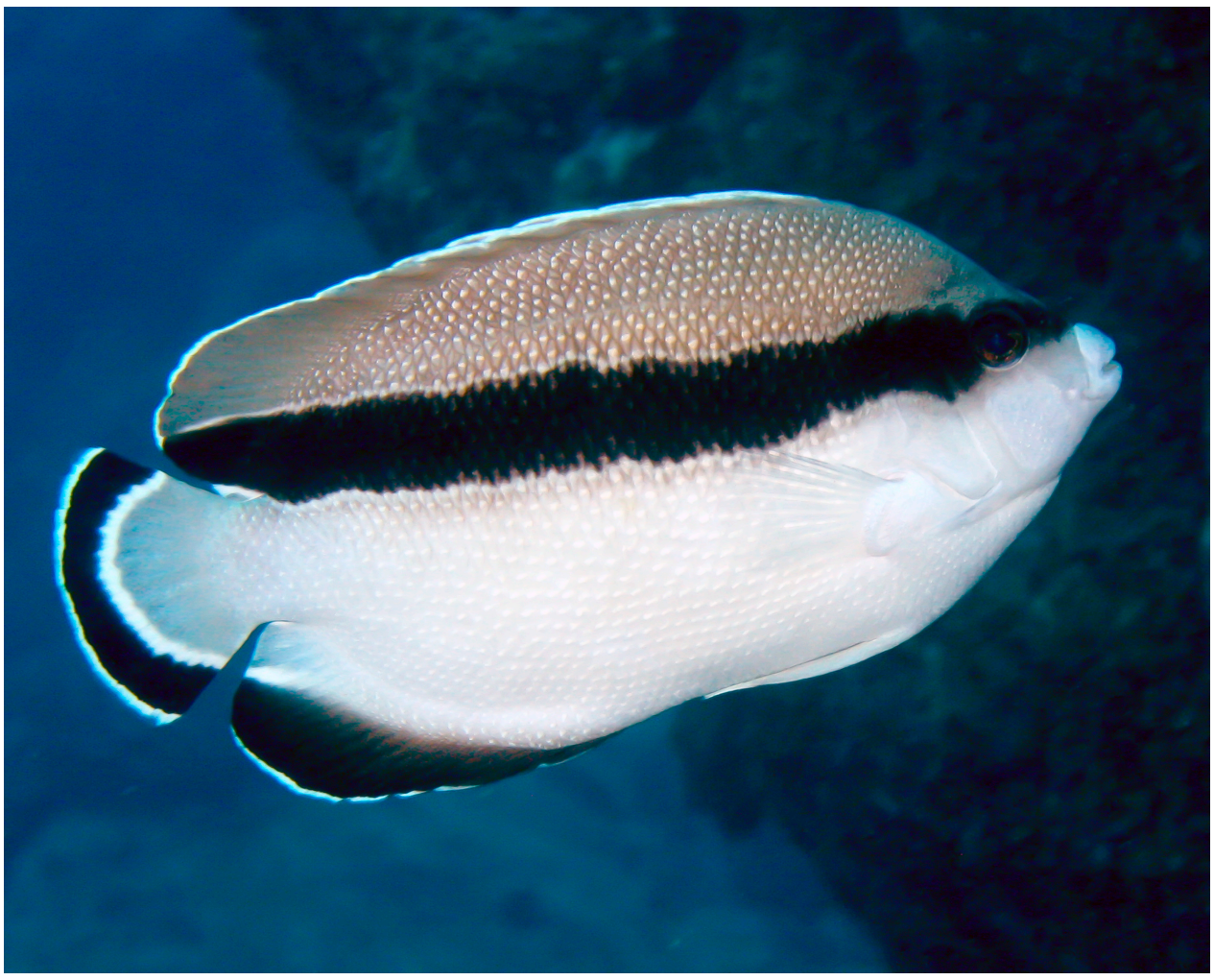
Then the sample is monitored for as the nuclear spins "relax" back to +½ spin states. The emitted photons are analyzed using a mathematical technique called to extract frequency and intensity information. The frequency and intensity information is used to plot the spectrum on the ppm scale.

Z. The Fourier transform converts the emitted photon data into component wavelength and intensity information that is plotted on the ppm scale.











MRI – Nuclear Magnetic Resonance Imaging – Produces a 3-d image inside the body.

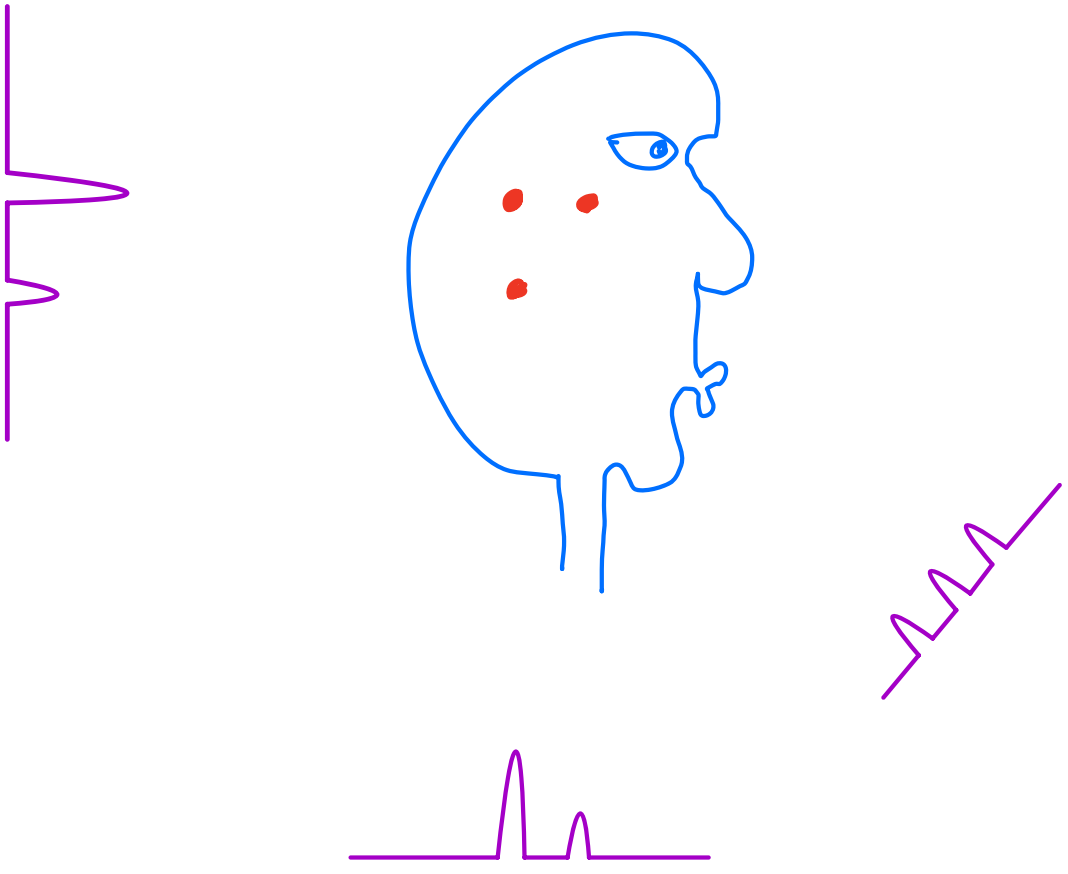
MRI is similar in approach, but complementary to, a CAT scan, which uses X-rays for imaging.

MRI is therefore safer than a CAT scan (no X-rays or other damaging radiation is used). Radiofrequency electromagnetic radiation does not cause DNA damage or any other kind of damage.

MRI primarily visualizes soft-tissue and especially cancer tumors while a CAT scan primarily visualizes bones or Calcium based dyes drunk to visualize the digestive tract.

MRI uses the same principles and NMR.

1) The patient is placed in a very strong magnetic field. Creating this very strong magnetic field is technically very demanding, explaining MRI machines are so expensive (~ 0.5 – 1.5 $ million)
2) The patient is irradiated with radiofrequency electromagnetic radiation.
3) The flipping (resonance) of 1H nuclear spins is monitored – Actually emitted photons are measured using the FT method.
4) Magnetic field gradients are used to gain imaging information. The magnetic field gradients are rotated around a central point and measurements are taken at each angle around 360° to gain 2-dimensional information. This technique is called **tomography**.



The overall MRI imaging approach involves looking at each 2-dimensional slice.

Each slice is added to give a 3-dimensional stack (analogous to stacking DVD's or CD's).

Each slice is shaded to indicate differences in the amount of ^{1}H atoms in different areas/tissues.

Water and fat have the highest density of ^{1}H atoms, so these are primarily being monitored in an MRI image.

The popular medical diagnostic technique of magnetic resonance imaging (MRI) is based on the same principles as NMR, namely the flipping (i.e. resonance) of nuclear spins of H atoms by radio frequency irradiation when a patient is placed in a strong magnetic field. Magnetic field gradients are used to gain imaging information, and rotation of the gradient around the center of the object gives imaging in an entire plane (i.e. slice inside patient). In an MRI image, you are looking at individual slices that when stacked make up the three-dimensional image of relative amounts of H atoms, especially the H atoms from water and fat, in the different tissues [Memorize the preceding passage, as it will be worth 14 points on the final. No I am not kidding, 14 points right there.]

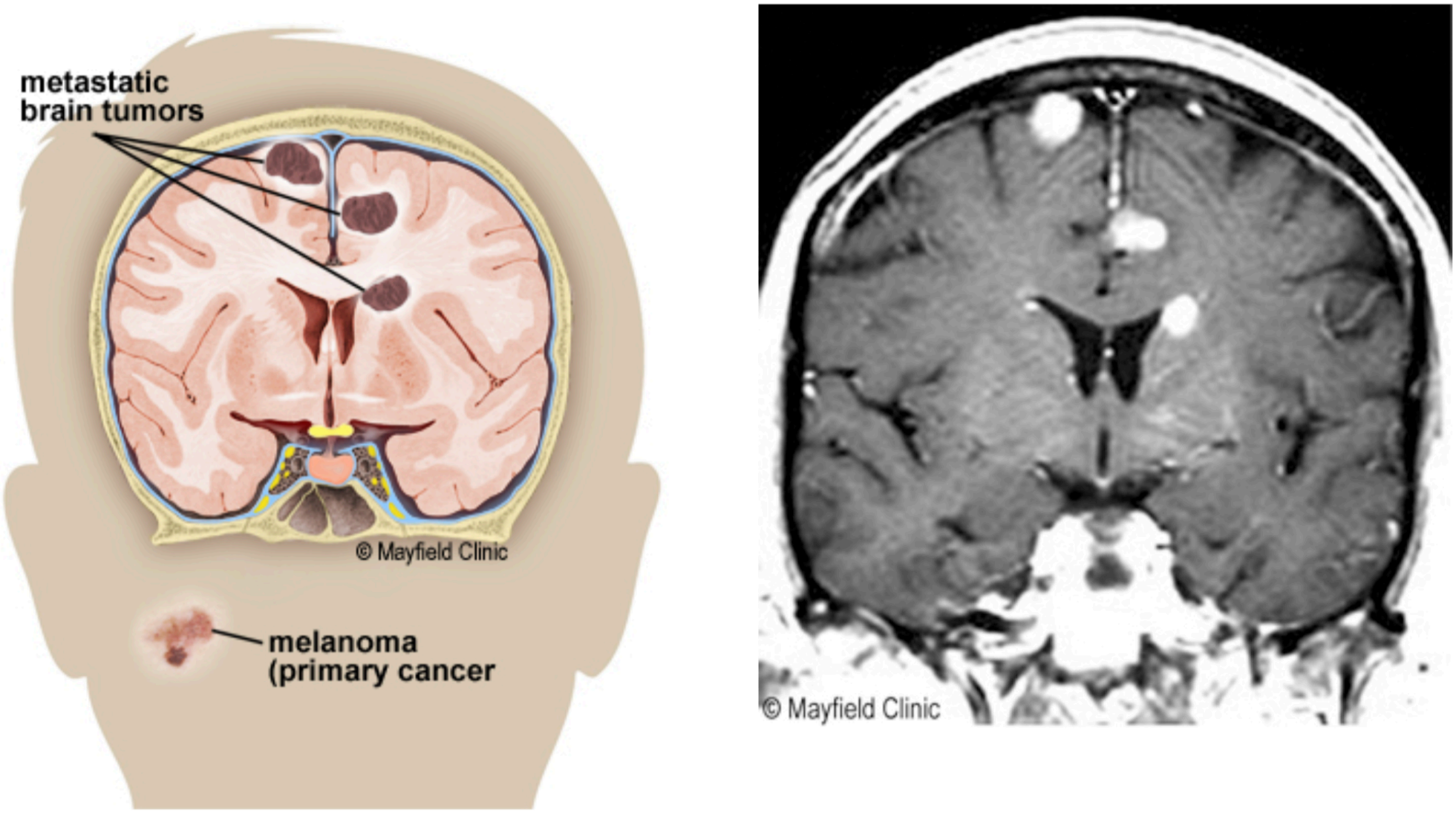
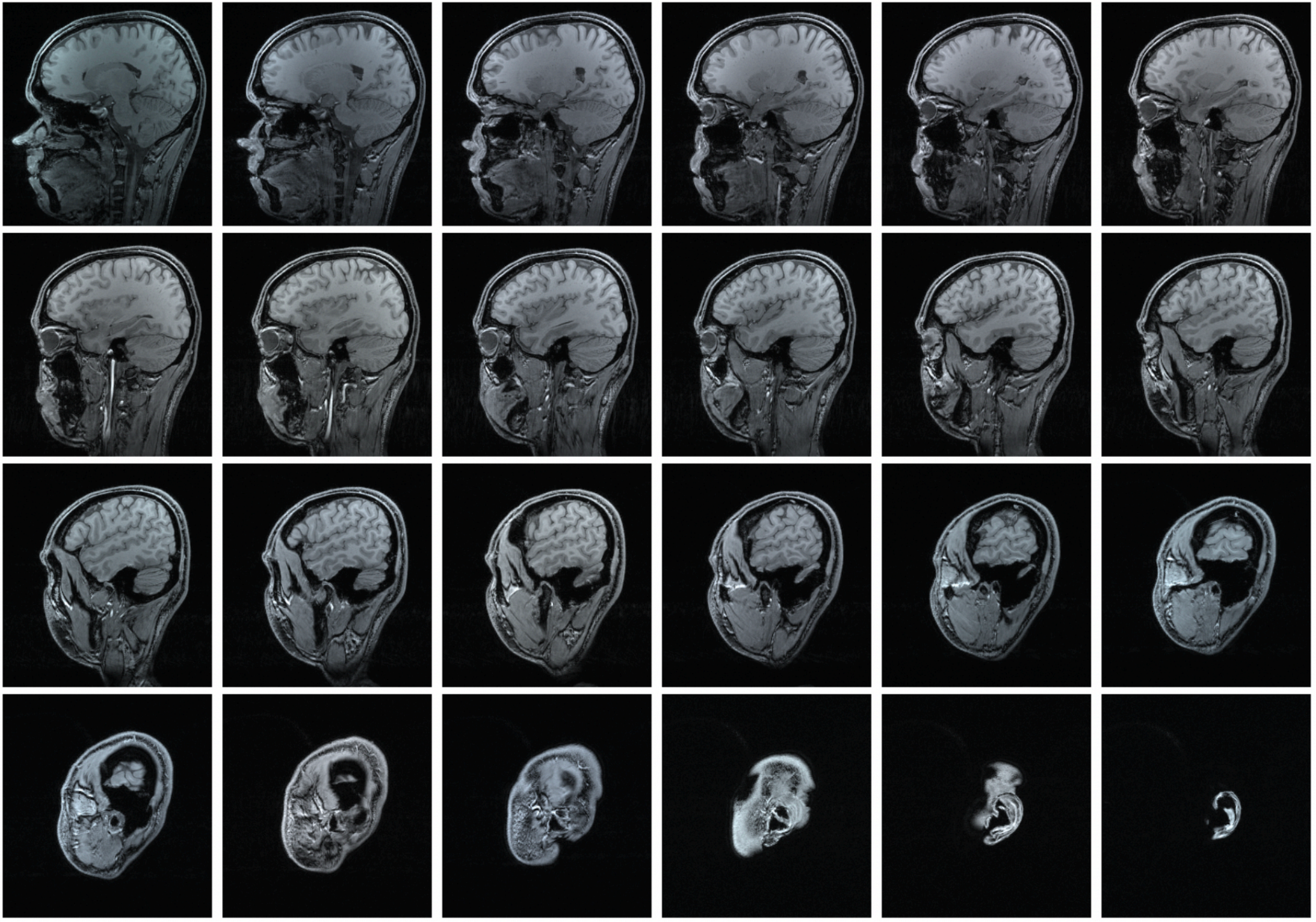


Figure 1. Illustration and MRI of multiple metastatic brain tumors that have spread from the melanoma skin cancer on the face.



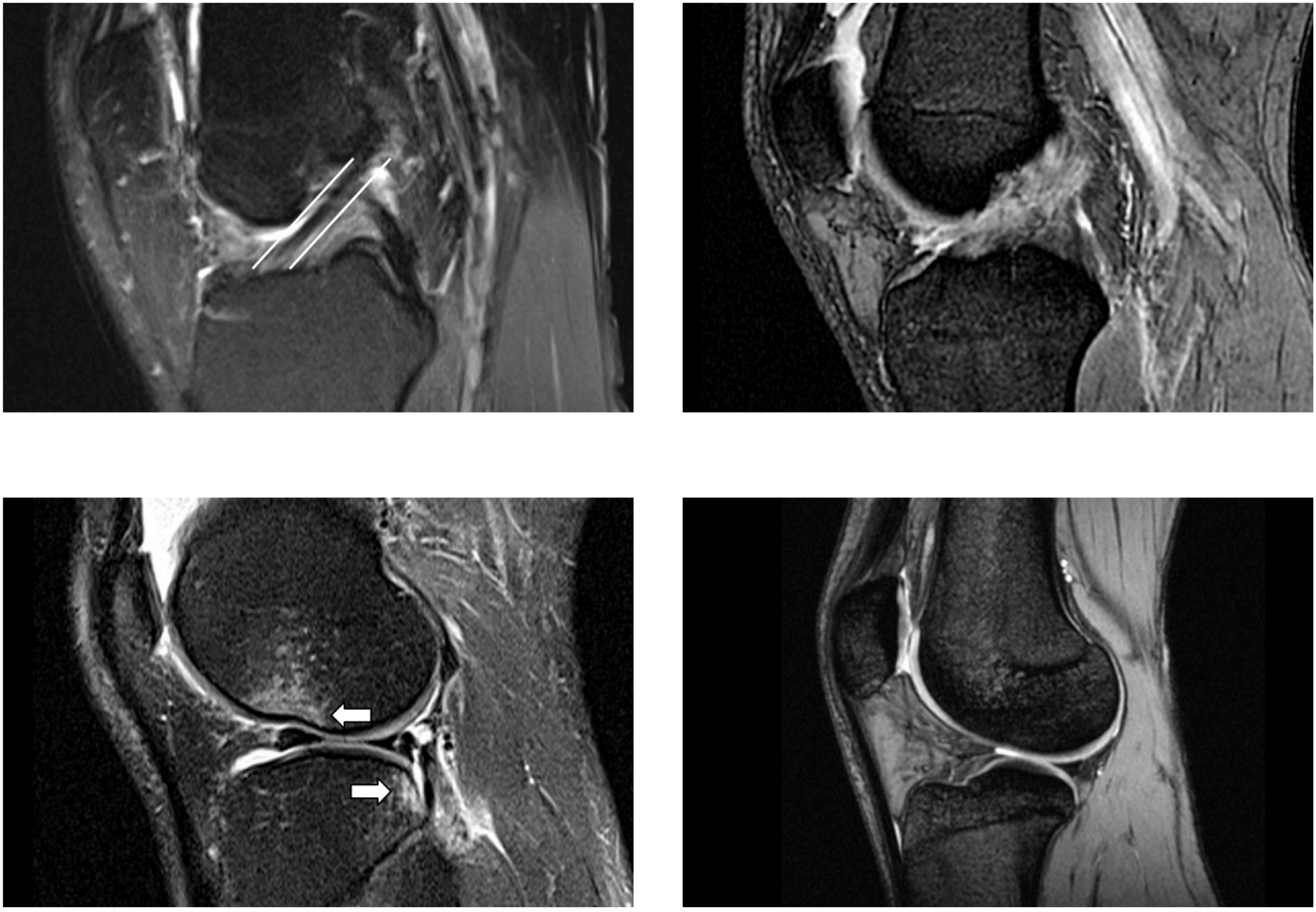


Image 13-16: MRI images of a normal ACL (between white lines), ruptured ACL (ligament not clearly visible), bone marrow oedema (white arrows) and anterior tibial translation.

The Amide Bond Shows Up in Medical School
Monday, August 25

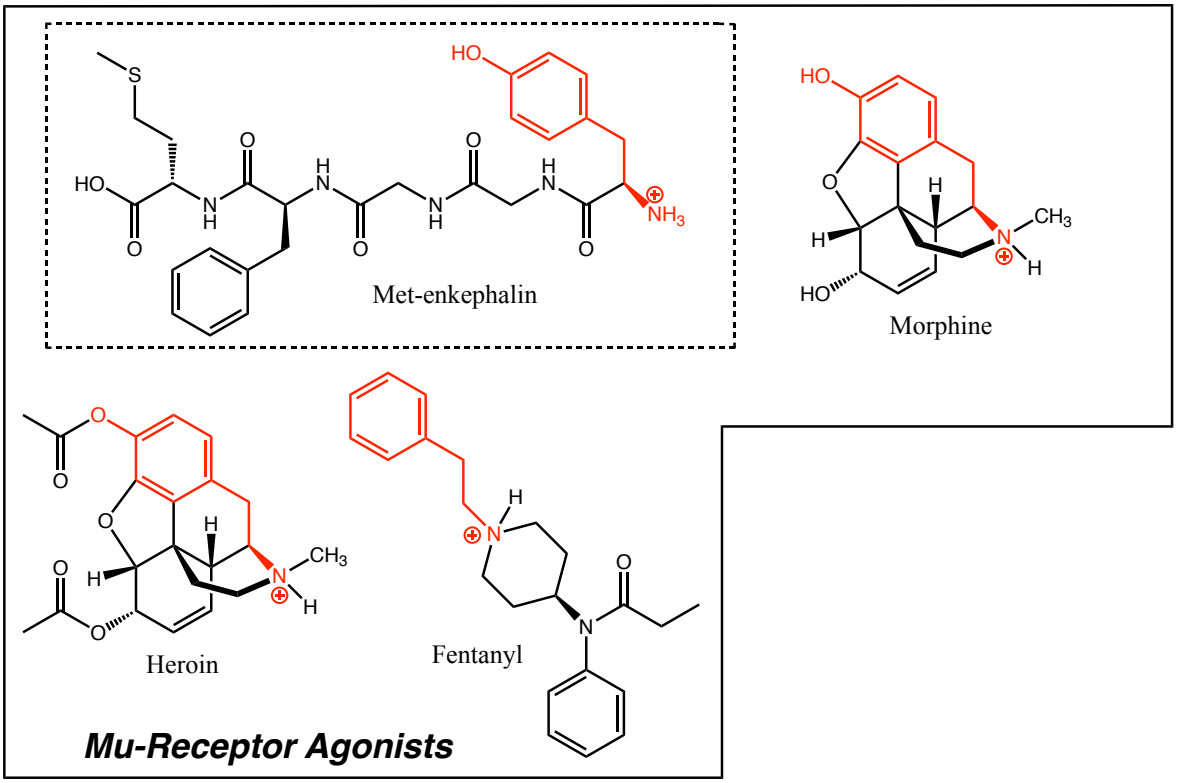
Hi Dr. Iverson,
I just wanted to share a little story from my first week of medical school:

The other day in my biochemistry lecture, the professor mentioned factors that gave proteins stability, including the double bond nature of the peptide bonds. That idea sounded strangely familiar until I realized I'd already memorized it earlier when you made us write out all the contributing structures of amides on every exam!

In just the first week of med school I've had several moments like this where topics mentioned in your class have helped speed up my understanding (MRI, enzyme mechanisms, etc.). I never expected so many details of an organic chemistry course to play small but important roles in medical sciences.

Thank you for taking the time to make your class relevant for all the pre-health professions students in your class!


m- m...
he's about to say his first words
The popular medical diagnostic technique of magnetic resonance imaging (MRI) is based on the same principles as NMR, namely the flipping (i.e. resonance) of nuclear spins of H atoms by radio frequency irradiation when a patient is placed in a strong magnetic field. Magnetic field gradients are used to gain imaging information, and rotation of the gradient around the center of the object gives imaging in an entire plane (i.e. slice inside patient). In an MRI image, you are looking at individual slices that when stacked make up the three-dimensional image of relative amounts of H atoms, especially the H atoms from water and fat, in the different tissues.



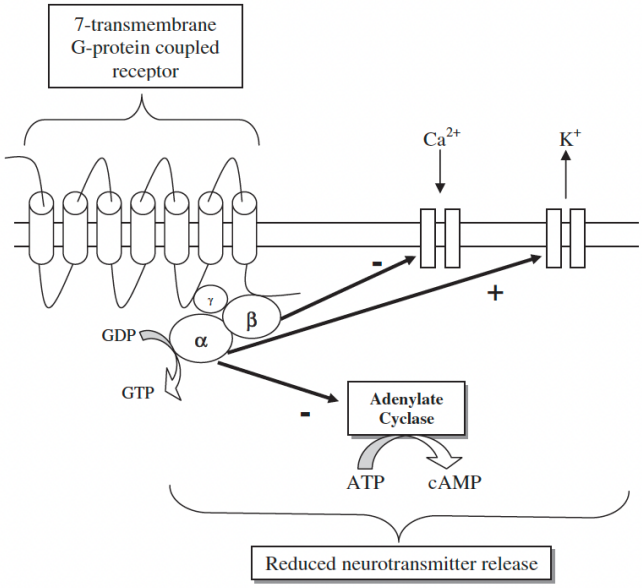


Fig. 1 Seven transmembrane structure of opioid G-protein-coupled receptor. Receptor activation by opioid receptor ligands leads to initiation of intracellular transduction pathways that include stimulation of potassium efflux, inhibition of VSCCs and inhibition of adenylyl cyclase. In this diagram the G-protein is denoted α, β, γ but the α-subunit interacts with K^+/Ca^{2+} channel and adenylate cyclase.

 DOI 10.1093/bjaceaccp/mki004
© The Board of Management and Trustees of the British Journal of Anaesthesia 2005

Fentanyl activates μ-opioid receptors (Gi/o-coupled) on GABAergic interneurons in the VTA, decreasing their cAMP levels and suppressing GABA release.

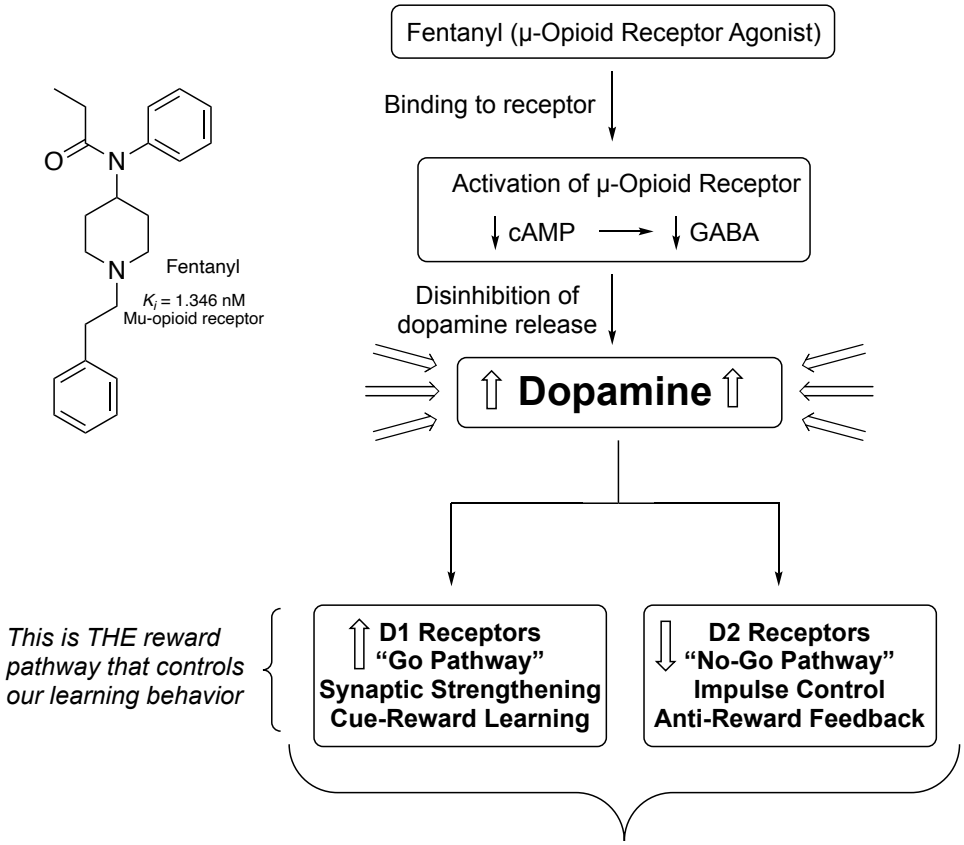
This disinhibits dopamine neurons and drives a surge of dopamine release into the nucleus accumbens.

Dopamine then acts on **D1 receptors** (Gs-coupled) to increase cAMP/PKA/CREB signaling, producing synaptic potentiation and strong reinforcement of fentanyl-associated cues.

In parallel, chronic fentanyl use **downregulates D2 receptor** (Gi/o) signaling, which normally provides inhibitory control and reduces compulsive reward seeking.

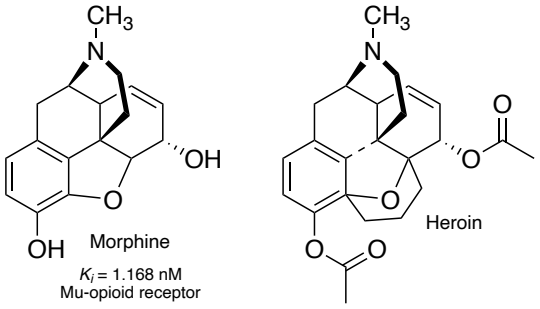
The combined effect—**D1 sensitization plus D2 suppression**—shifts basal ganglia signaling toward reward acquisition, producing the neurochemical basis of fentanyl addiction and relapse vulnerability.

Fentanyl triggers addiction by disrupting the brain's normal reward and control systems. It activates opioid receptors in a part of the brain that normally keeps dopamine release in check, effectively **removing the brakes** and causing a strong surge of dopamine—the chemical that signals pleasure and reward. This dopamine then acts on two types of receptors. **D1 receptors** amplify the brain's "go" signals, strengthening the memory and motivation to use the drug again. **D2 receptors**, which normally help with self-control and resisting impulses, become less active with repeated fentanyl use. As D1 activity becomes stronger and D2 activity becomes weaker, the brain becomes increasingly wired to seek fentanyl while losing the ability to hold back, creating the powerful cycle of addiction.



An individual is driven to pursue the drug and cannot anticipate negative consequences of drug use

---



PRESS RELEASE

13 Arrested in Connection with an LSD, Fentanyl and Methamphetamine Trafficking and Money Laundering Scheme Occurring in the West Campus Area of the University of Texas at Austin

Friday, December 4, 2020

Share

For Immediate Release

U.S. Attorney's Office, Western District of Texas





Click to download the full image

Authentic Xanax® Front and Back



Click to download the full image

Counterfeit Xanax® Front and Back

This is what a lethal dose of fentanyl looks like.



MARKETPLACE
Search For & Place Classifieds

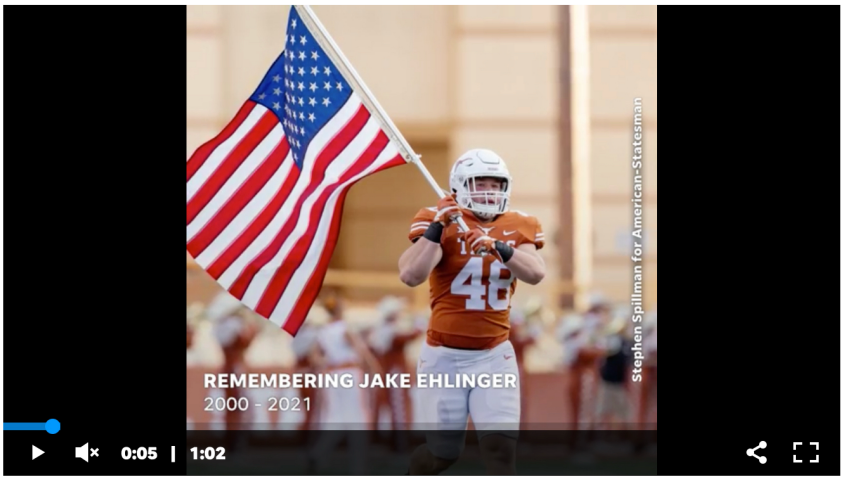
Austin American-Statesman
SERVING OUR COMMUNITY SINCE 1871

Jake Ehlinger's family releases statement saying Texas player died of accidental overdose



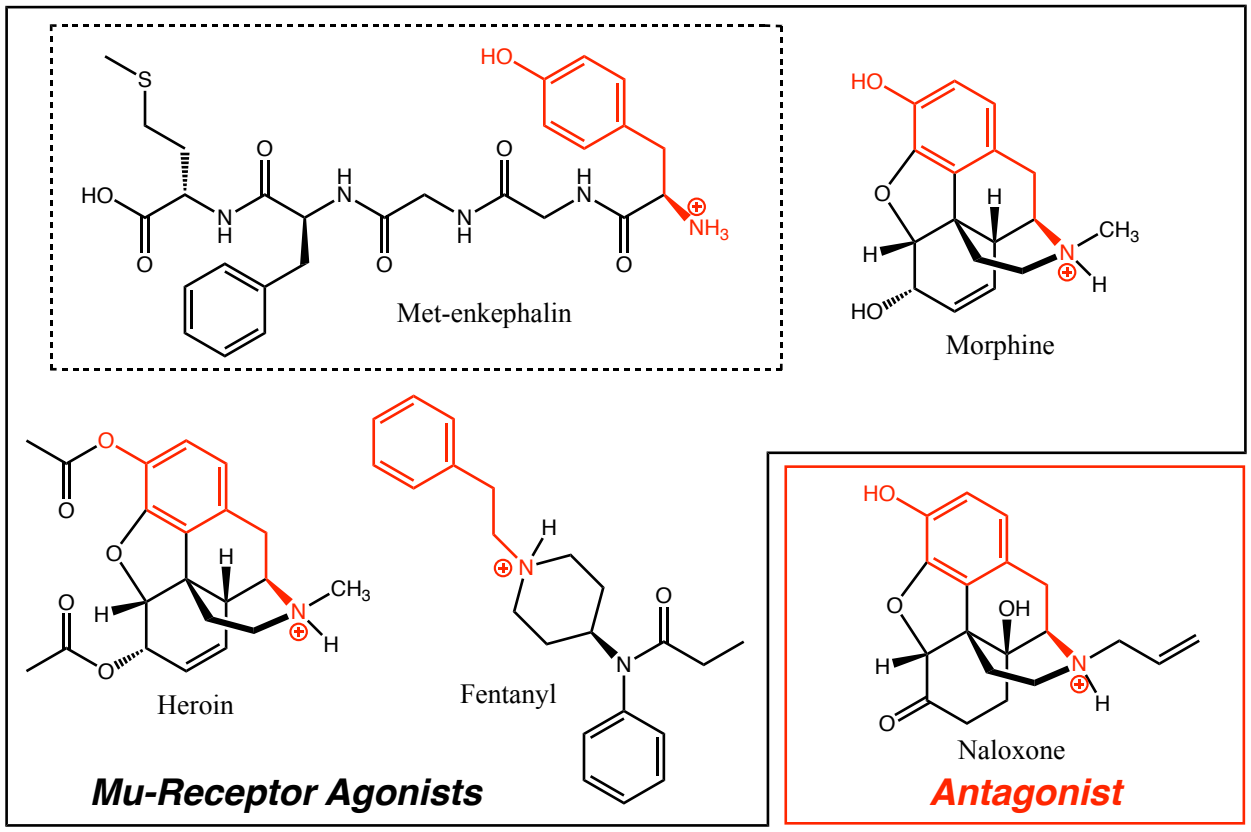
Brian Davis
Hookem

Published 4:56 p.m. CT Oct. 21, 2021 | Updated 3:54 p.m. CT Oct. 22, 2021



Remembering Texas linebacker Jake Ehlinger

Jake Ehlinger, younger brother of former Longhorns quarterback Sam Ehlinger, was found dead on May 6, Austin police said. *Austin American-Statesman*


Met-enkephalin
Morphine
Heroin
Fentanyl
Mu-Receptor Agonists
Naloxone
Antagonist


NARCAN® NASAL SPRAY – ANYONE CAN SAVE A LIFE
Be ready – at home or on the go. NARCAN® Nasal Spray is a treatment designed to rapidly reverse the effects of a life-threatening opioid emergency. Available as an over-the-counter medicine.
Original Prescription Strength
Easy to Use
Can Save a Life
NARCAN®
Naloxone HCl Nasal Spray 4 mg
Emergency Treatment of Opioid Overdose
Designed to Rapidly Reverse the Effects of a Life-Threatening Opioid Emergency
2 Single-Dose Nasal Spray Devices
0.003 fl oz (0.1 mL) each
For use in nose only

SHIFT
THE CAMPUS CULTURE

OPERATION NALOXONE

Availability of Narcan on campus:

EMERGENCY USE: Originally placed in all residence halls; carried by UTPD; in the libraries across campus, Sid Richardson Hall, (Strategically covers all areas of our large campus)

DISTRIBUTION: Original site was the main PCL library (late night center of social/academic activity); Anyone can obtain a free box of Narcan Nasal Spray (2 doses) from the security desk no questions asked.

Hi Dr. Iverson,

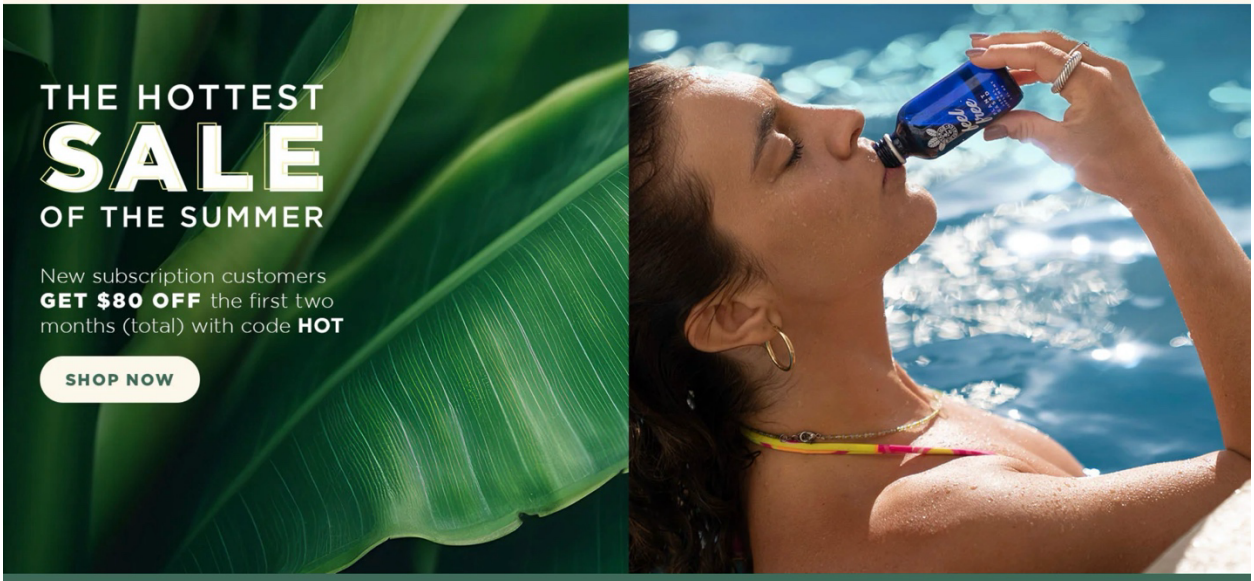
I graduated with a BSA in Neuroscience in May 2023, and you were my organic chemistry professor during COVID! During your class, you shared about Operation Naloxone at UT Austin which was instrumental in my life when I was in need of Narcan a few years later for my loved one battling addiction...

> Day 1 was the day I found out he was using drugs recreationally since the age of 13. Year 6 was the year I accepted his substance abuse as a progressive illness. The darkness that lured him in changed my life forever when he disappeared one night and under the influence called our mom to let her know he was lost, the call disconnecting shortly after. I was afraid to know the substances he used, but one day with my heart ringing in my ears, I asked. This is how I knew I needed to request narcan from the free distribution services at my university that night. I tracked his last location on our shared family app and without knowing where or to what I was headed my mom and I drove to him. With shaking hands I read the narcan instructions and prepared for the worst. In the distance, I could see my brother's car and I could see his face and head resting back onto the driver's seat. The rest of the event's that night are oddly blurry yet so clearly ingrained in my memory. I remember having to put his car in park, trying to wake him up unsuccessfully, shouting out to my mom to call 911, using the Narcan, his eyes suddenly opening wide and him taking a deep breath in. Today, my brother is recovering after years of battling anxiety, depression, and substance abuse. His experiences from childhood to adulthood have been a driving force in my research endeavors and education in neuroscience.

I am grateful for the impact you have had on my academic journey and wanted to share this part of my story with you. Thank you for your inspiration and guidance!

Best,

SHOP ONLINE STORE LOCATOR LEARN PRESS



"The head is affected pleasantly; you feel friendly, not beer sentimental; you cannot hate with kava in you. Kava quiets the mind; the world gains no new color or rose tint; it fits in its place and in one easily understandable whole."

- Tom Harrison, author

enjoy *feel free*® products when you want:



A CLEAN ENERGY BOOST WITHOUT THE JITTERS



A SOCIAL LIFT WITHOUT THE BOOZE (OR HANGOVER)



A FOCUS ENHANCEMENT WITHOUT THE CRASH

shop *feel free*® products



feel free tonic

SHOP NOW



CLASSIC tonic

SHOP NOW



CLASSIC capsules

SHOP NOW

× Where can I find nutritional information?

Please find our supplement facts below. Feel free to ask any questions you may have by emailing hi@botanictonics.com.

feel free® CLASSIC

TONIC

Supplement Facts
Serving Size: 1 fl oz (29.6 mL)
Servings Per Container: 2

	Amount Per Serving	%DV
Iron	0.4 mg	4%#
Kava root (extract)		
Total Kavalactones	260 mg	*
Kratom leaf (ground)		
Total Alkaloids	34 mg	*
Mitragynine	20 mg	*
7-hydroxymitragynine	<0.05 mg	*

#Daily Value (DV) based on a 2000 calorie diet
*Daily Value (DV) not established

Other ingredients: water, pineapple juice, natural flavors, stevia leaf, citric acid.

CAPSULE BOTTLE

Supplement Facts
Serving Size: 3 capsules
Servings Per Container: 30

	Amount Per Serving	%DV
Iron	0.4 mg	4%#
Kava root (extract)		
Total Kavalactones	210 mg	*
Kratom leaf (ground)		
Total Alkaloids	28 mg	*
Mitragynine	17 mg	*
7-hydroxymitragynine	<0.05 mg	*

#Daily Value (DV) based on a 2000 calorie diet
*Daily Value (DV) not established

Other ingredients: vegan capsule, calcium stearate

CAPSULE CASE

Supplement Facts
Serving Size: 3 capsules
Servings Per Container: 24

	Amount Per Serving	%DV
Iron	0.4 mg	4%#
Kava root (extract)		
Total Kavalactones	210 mg	*
Kratom leaf (ground)		
Total Alkaloids	28 mg	*
Mitragynine	17 mg	*
7-hydroxymitragynine	<0.05 mg	*

#Daily Value (DV) based on a 2000 calorie diet
*Daily Value (DV) not established

Other ingredients: vegan capsule, calcium stearate

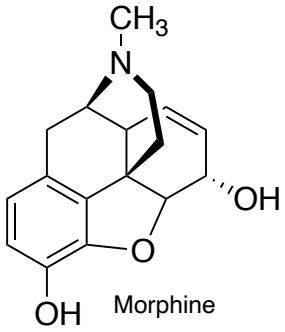
feel free®

Supplement Facts
Serving Size: 1 fl oz (29.6 mL)
Servings Per Container: 2

Amount Per Serving		% Daily Value
Calories	15	
Total Carbohydrate	4 g	1.5%†
Total Sugars	4 g	*
Includes 4 g Added Sugars		8% †
Proprietary Blend	1800 mg	*
Kava root (extract), Kola nut (extract), Lion's Mane Mushroom fruitbody (extract), *Rhodiola rosea* seed (extract)		
Caffeine (from Kola nut)	100 mg	*

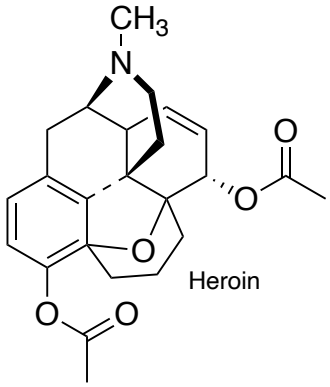
† Percent Daily Values are based on a 2,000 calorie diet
* Daily Value (DV) not established

Other ingredients: water, organic cane sugar, MCT powder, natural flavors, malic acid

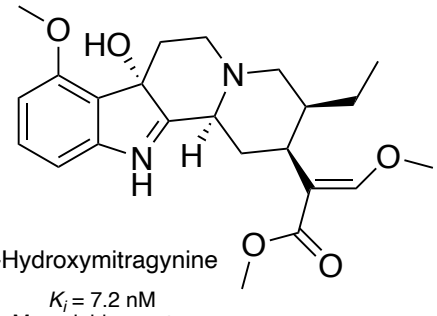


Morphine

K_i = 1.168 nM
Mu-opioid receptor



Heroin



7-Hydroxymitragynine

K_i = 7.2 nM
Mu-opioid receptor

Regulatory Toxicology and Pharmacology
Volume 59, Issue 3, April 2011, Pages 385-390

ACS Chem. Neurosci. 2023, 14, 195–197

ADVERTISEMENT


Judge awards $11 million to family in death of Boynton Beach woman from kratom

Krystal Talavera, a mother of four who lived in Boynton Beach, died in 2021





PLOT TWIST!

Ships within 5 business days
Free shipping for every U.S. order
Money back guarantee

PLANT BASED · 100% VEGAN · LAB TESTED · KOSHER CERTIFIED · ALCOHOL FREE · NUT FREE · GLUTEN FREE

“It gives a very nice light feeling, like life is a little more effortless”

Official Tonic of FSU ATHLETICS

Official Tonic Sponsor of TEXAS ATHLETICS



NEVER buy black market

or other pharmaceuticals → it is not black market it is counterfeit and contains Fentanyl ⇒ Could be fatal !!

↓

Xanax

or methamphetamine ⇒ Highly addictive

↓

Adderall

You should know where to find Naloxone (Narcan) in case you need it to save a life!

⇒ RAs, Dorms, Libraries

⇒ Contact SHIFT



Naloxone (Narcan) is an antagonist to opioid receptors

Does not cause a reaction but blocks drugs like fentanyl from binding and activating the receptor

THE NEW YORK TIMES, TUESDAY, JANUARY 31, 1995

AIDS Is Now the Leading Killer of Americans From 25 to 44

By LAWRENCE K. ALTMAN

Special to The New York Times

WASHINGTON, Jan. 30 — AIDS has become the leading cause of death among all Americans aged 25 to 44, new Federal data show. The data were reported for the first time at a scientific meeting here today.

AIDS surpassed unintentional injury, the Government's category for accidents, which dropped to second place in this age group, said Dr. Harold W. Jaffe, a top AIDS official at the Federal Centers for Disease Control and Prevention in Atlanta. Cancer and heart disease were third and fourth, followed by homicides and suicides.

"AIDS was expected to rise to the top of the list eventually, but no one had predicted which year," Dr. Jaffe said in an interview at a meeting on human retroviruses and related infections.

The importance of the heterosexual AIDS epidemic cannot be ignored.

The AIDS curve for deaths among Americans from 25 to 44 has risen steadily and steeply since the disease was first recognized in 1981. "The dramatic rise is due to the accumulating toll from AIDS and is almost certain to continue because AIDS deaths reflect infections from H.I.V., the AIDS virus, that were acquired several years earlier," Dr. Jaffe said.

The tabulations were based on preliminary analysis of data for 1993, the latest year available, Dr. Jaffe said.

AIDS became the leading cause of death ar
1992. It r
en, behin
ries and
ed to re
rise to s
next fe
surpass
among

More
includin
children
centers
recogni
have die
ed cause
have be
age gro

AIDS
death in
Americ
greater
women,
cause o
cities. T
ven and
ter, Ma
York Ci

SAN DIEGO COUNTY

Los Angeles Times

CIRCULATION: 1,242,864 DAILY / 1,576,425 SUNDAY
FRIDAY, NOVEMBER 8, 1991
DAILY 35¢
AN EDITION OF THE LOS ANGELES TIMES

COLUMN ONE

A Ghostly Shiver in Cambodia

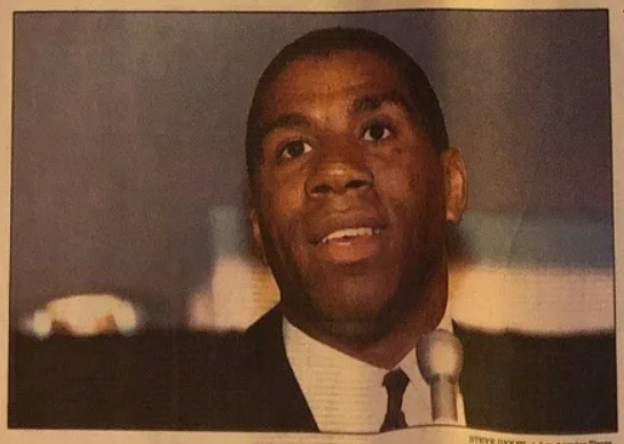
■ An end to civil war may give the Khmer Rouge, which left 1 million people dead in the '70s, a second chance at power. The despotic Pol Pot is believed to be pulling the strings.

By CHARLES P. WALLACE
TIMES STAFF WRITER

ARANYAPRATHET, Thailand—"The Khmer Rouge," said the Buddhist monk, nervously adjusting his saffron robes, "is like a creature with two faces. The face we can see is good, but the face we cannot see is evil. That is why all Cambodians are still afraid."

On the one hand, he explained, there is Khieu Samphan, a dapper, French-educated economist who is now the official leader and spokesman for the pro-Chinese guerrilla group. Khieu Samphan apologetically wants to let "bygones be bygones" and speaks of the need for a "liberal democratic, pluralistic regime with a free-market economy" in a future Cambodia.

But the "other face" of the Khmer Rouge is Pol Pot, the chauvinistic, ultra-orthodox Communist whose rule in Cambodia from 1975 to early 1979 left more than 1 million people dead from



STEVE DYKES / Los Angeles Times

Lakers' Earvin (Magic) Johnson announces his retirement at a press conference after testing HIV-positive.

Magic Johnson's Career Ended by HIV-Positive Test

■ **Sports:** The announcement stuns his public. The Lakers star emphasizes that he does not have AIDS. 'I plan to go on living for a long time,' he says.

By MARK HEISLER, TIMES STAFF WRITER

With an announcement that stunned the nation, Earvin (Magic) Johnson, the brilliant guard who was the marquee name for the Lakers and the National Basketball Assn. for 12 years, retired Thursday, saying he had tested positive for the virus that causes AIDS.

Johnson, 32, was characteristically upbeat when he made the announcement at a packed press conference at the Forum in Inglewood.

Flashing his trademark smile, he stressed that while he is infected with the human immunodeficiency virus, he has not developed AIDS. Johnson said he intends to remain active in basketball off the court and that he will become a spokesman for AIDS prevention.

"I plan to go on living for a long time. . . ," he said.

"I'm going to be a spokesman for the HIV virus. I want young people to realize they can practice safe sex. Sometimes you're a little naive about it and you think something like that can never happen to you. It has happened but I'm going to deal with it. My life will go on. Life is going to go on and I'll be a happy man.

". . . It's another challenge, another chapter in my life. My back is

An Icon Falls and His Public Suffers the Pain

By DEAN E. MURPHY and TINA GRIEGO
TIMES STAFF WRITERS

Magic Johnson took pains on Thursday to stress that he is very much alive, that being HIV-positive is not the same as having AIDS. But the part of him that was pronounced dead—his presence on the basketball court—had held Southern California so spellbound for so long that a funereal pall descended.

An icon had been shot down in

Heeding Bush, NATO Backs Lead Role by U.S.

■ **Europe:** His blunt message forces formal recognition of a continuing pre-eminent American position.

By JAMES GERSTENZANG and WILLIAM TUOHY
TIMES STAFF WRITERS

ROME—In unusually blunt lan- delivered behind closed doors and relayed by a senior White House official, was concern that three developments—revitalization of the Western European Union,

FDA Likely to Speed Approval of New Drugs

By MARLENE CIMONS
TIMES STAFF WRITER

WASHINGTON—The Food and Drug Administration is expected to implement a series of reforms to dramatically shorten the time it

PERSPECTIVE

OBC
www.rsc.org/obc

HIV-1 protease: mechanism and drug discovery

Ashraf Brik and Chi-Huey Wong *
Department of Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA

Received 22nd August 2002
First published as an Advance Article on the web 26th November 2002

1 Introduction

It has now been two decades since acquired immunodeficiency syndrome (AIDS) was first reported by the US Center for Diseases Control (CDC). A few years later, it was found that a retrovirus called human immunodeficiency virus (HIV) is the causative agent in AIDS.[1] In a short time, AIDS increased to epidemic proportions throughout the world, affecting more than 40 million people today and killing so far more than 22 million (UNAIDS, 2001).

Since the outbreak of the AIDS epidemic, tremendous efforts have been directed towards development of antiretroviral therapies that target HIV type 1 in particular (HIV-1). The identification of the HIV retrovirus and the accumulated knowledge about the role of the different elements in its life cycle led researchers around the world to develop inhibitors that target different steps in the life cycle of the virus. One of these targets is HIV-1 protease (HIV PR), an essential enzyme needed in the proper assembly and maturation of infectious virions. Understanding the chemical mechanism of this enzyme has been a basic requirement in the development of efficient inhibitors. In this review, we summarize studies conducted in the last two decades on the mechanism of HIV PR and the impact of their conclusions on the drug discovery processes.

2 The life cycle of HIV

HIV belongs to the class of viruses called retroviruses, which carry genetic information in the form of RNA. HIV infects T cells that carry the CD4 antigen on their surface. The infection of the virus requires fusion of the viral and cellular membranes, a process that is mediated by the viral envelope glycoprotein (gp120, gp41) and receptors (CD4 and coreceptors, such as CCR5 or CXCR4) on the target cell. As the virus enters a cell, its RNA is reverse-transcribed to DNA by a virally encoded enzyme, the reverse transcriptase (RT). The viral DNA enters the cell nucleus, where it is integrated into the genetic material of the cell by a second virally encoded enzyme, the integrase. Activation of the host cell results in the transcription of the viral DNA into messenger RNA, which is then translated into viral proteins. HIV protease, the third virally encoded enzyme, is required in this step to cleave a viral polyprotein precursor into individual mature proteins. The viral RNA and viral proteins assemble at the cell surface into new virions, which then bud from the cell and are released to infect another cell. The extensive cell damage from the destruction of the host's genetic system to the budding and release of virions leads to the death of the infected cells.

3 HIV protease

3.1 HIV protease: a logical target for AIDS therapy

Unless the HIV life cycle is interrupted by specific treatment, the virus infection spreads rapidly throughout the body, which results in the weakness and destruction of the body's immune system. From the analysis of the HIV life cycle, one could conclude that there are several steps that might be interfered with, thus stopping the replication of the virus. For example, there are several commercially available drugs that inhibit the enzyme reverse transcriptase (RT). The first class of RT inhibitors is the nucleoside analogs such as AZT, ddI, ddC and d4T. These dideoxy compounds lack the 3′-hydroxy, causing DNA chain termination when they are incorporated into the growing DNA strand. The second class of inhibitors is the non-nucleoside inhibitors (NNIs); these inhibitors are known to bind in a pocket away from the polymerase active site, and are believed to cause a conformational change of the enzyme active site, and thus inhibit its action. Currently, there are three available non-nucleoside reverse transcriptase inhibitors (nevirapine, delavirdine, and efavirenz) for the treatment of AIDS.

Another critical step in the life cycle of HIV is the proteolytic cleavage of the polypeptide precursors into mature enzymes and structural proteins catalyzed by HIV PR. It has been shown that budded immature viral particles that contain catalytically inactive protease cannot undergo maturation to an infective form.[2] The necessity of this enzyme in the virus life cycle makes it a promising target for therapy of the HIV infection.[3]

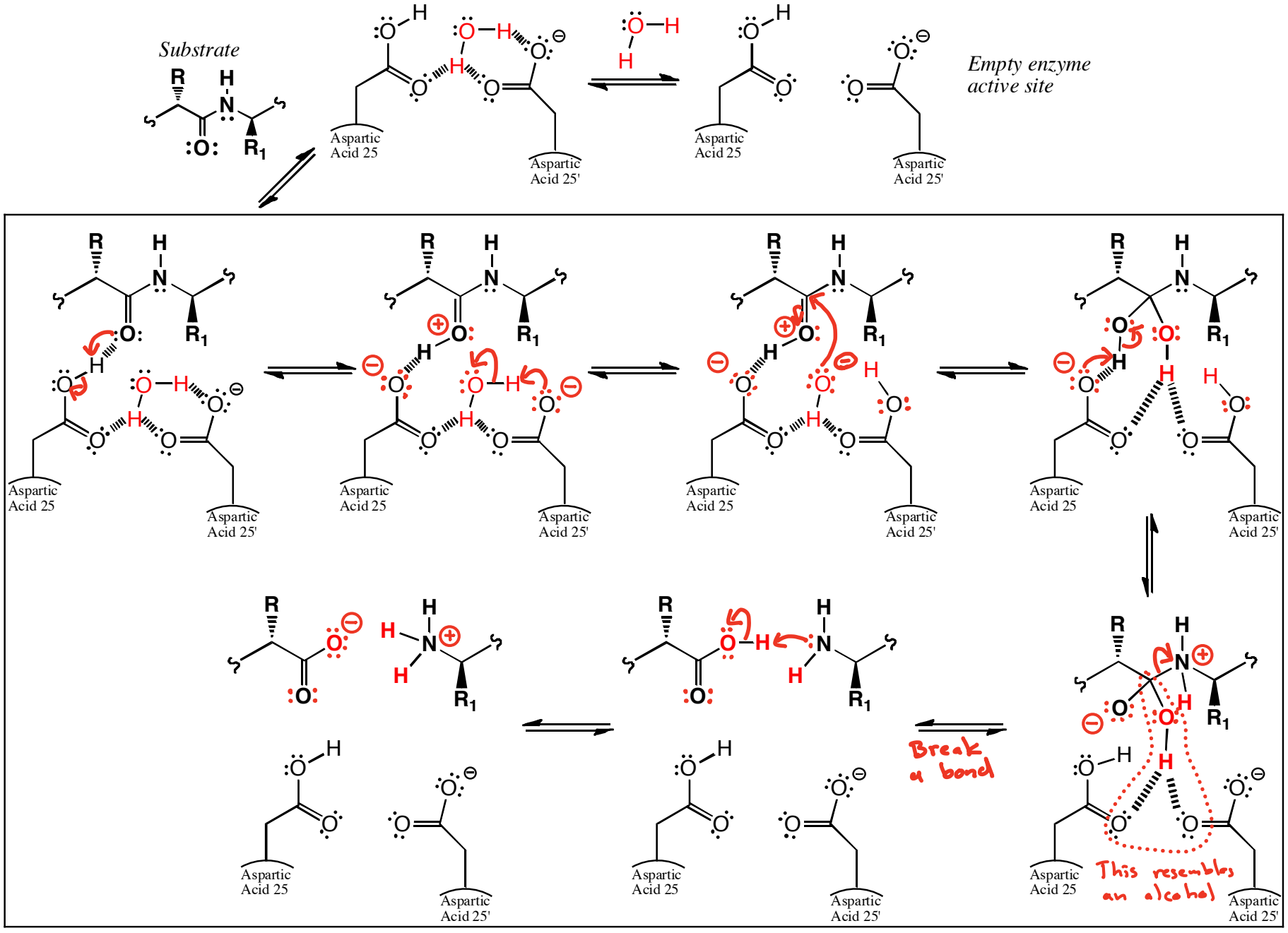
3.2 Structure of HIV protease

Navia *et al.* from Merck laboratories were the first group to obtain a crystal structure of HIV PR;[4] a more accurate structure was reported subsequently by Kent and coworker.[5] HIV PR is a 99 amino acid aspartyl protease which functions as a homodimer with only one active site which is C_2-symmetric in the free form. More than 140 structures of the HIV-1 PR, its mutants and enzymes complexed with various inhibitors have been reported so far. A database dedicated to providing structural information about HIV PR has been created at the National Cancer Institute (http://www-fbsc.ncifcrf.gov/HIVdb/). The enzyme homodimer complexed with TL-3[6] is shown in Fig. 1 (PDB ID: 3TLH). Each monomer contains an extended β-sheet region (a glycine-rich loop) known as the flap, that constitutes in part the substrate-binding site and plays an important role in substrate binding, and one of the two essential aspartyl residues, Asp-25 and Asp-25′ which lie on the bottom of the cavity. The substrate binds in its extended conformation, in which its interactions with the different amino



Fig. 1 Structure of HIV PR complexed with TL-3 (PDB: 3TLH).

DOI: 10.1039/b208248a


Substrate
Aspartic Acid 25
Aspartic Acid 25'
Empty enzyme active site
Break a bond
This resembles an alcohol

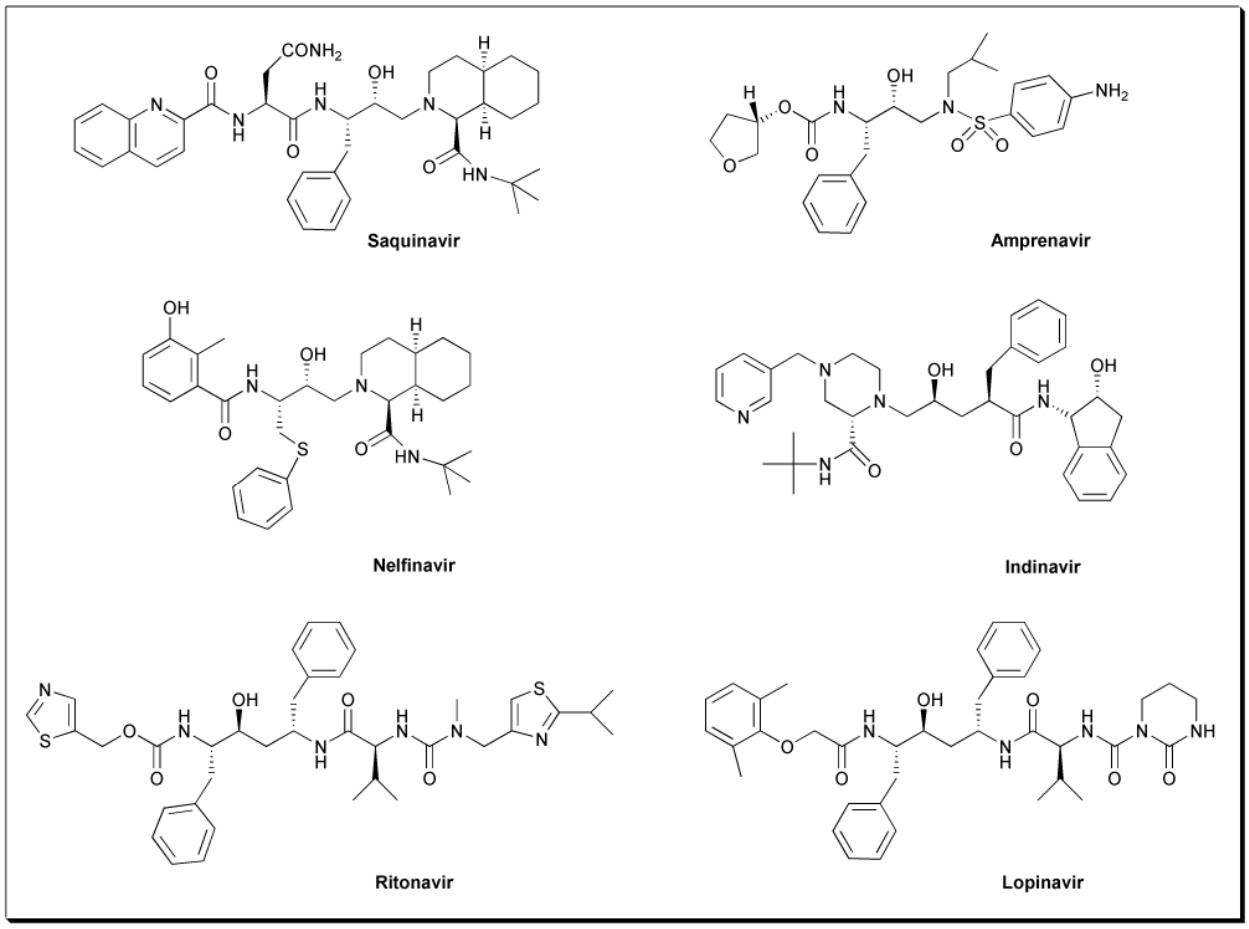


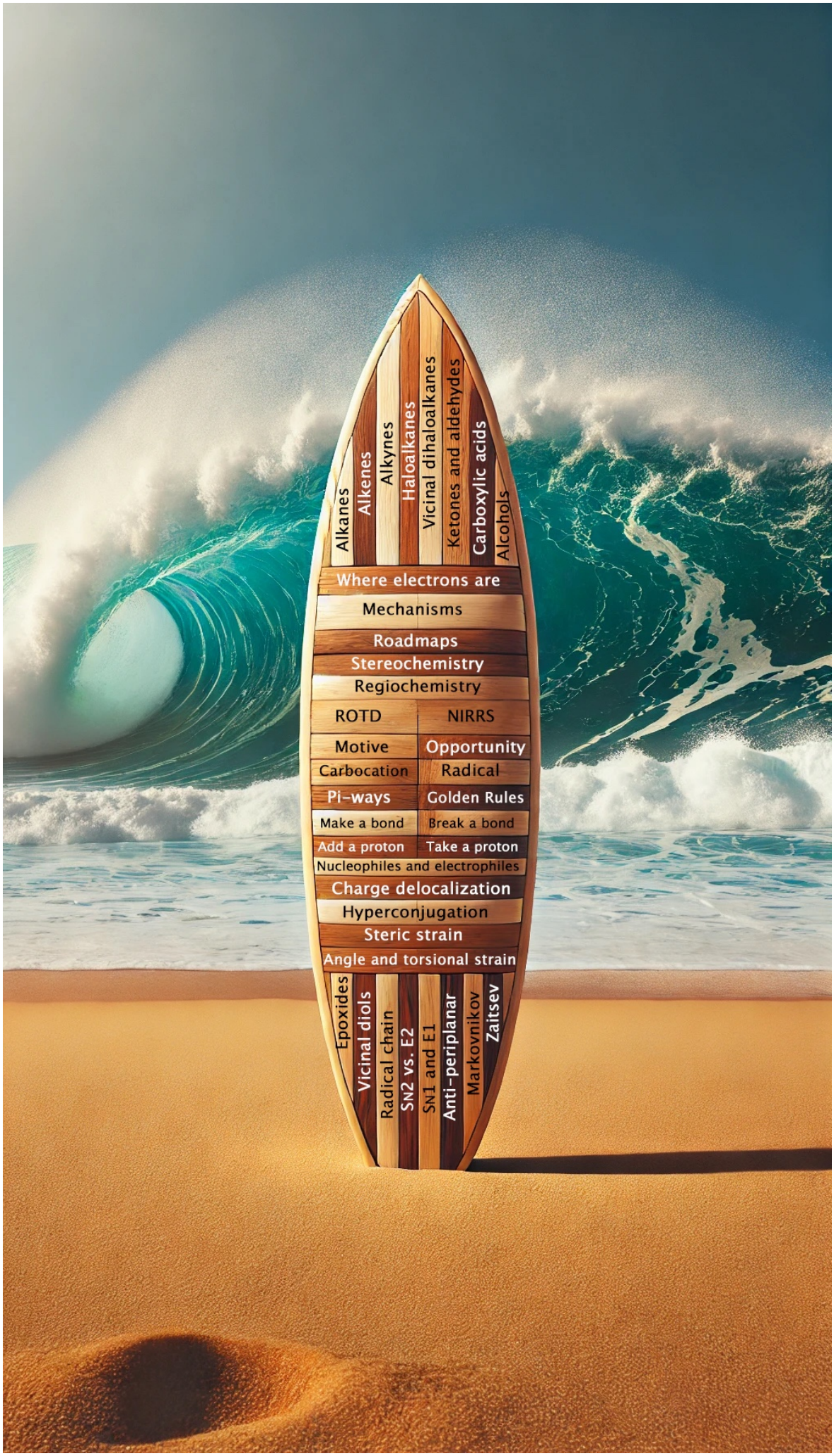
Fig. 10 FDA approved HIV-1 protease inhibitors.

These all have alcohol groups that resemble the -OH of the key tetrahedral intermediate seen in the enzyme reaction.

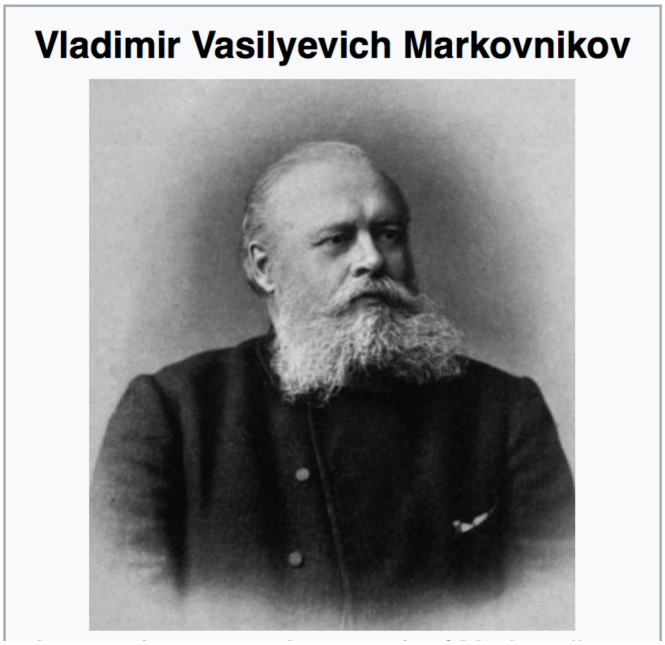


“You can’t stop the waves, but you can learn to surf”

Jon Kabat-Zinn


Alkanes
Alkenes
Alkynes
Haloalkanes
Vicinal dihaloalkanes
Ketones and aldehydes
Carboxylic acids
Alcohols
Where electrons are
Mechanisms
Roadmaps
Stereochemistry
Regiochemistry
ROTD
NIRRS
Motive
Opportunity
Carbocation
Radical
Pi-ways
Golden Rules
Make a bond
Break a bond
Add a proton
Take a proton
Nucleophiles and electrophiles
Charge delocalization
Hyperconjugation
Steric strain
Angle and torsional strain
Epoxides
Vicinal diols
Radical chain
SN2 vs. E2
SN1 and E1
Anti-periplanar
Markovnikov
Zaitsev

Vladimir Markovnikov



Alkenes are the very best, their reactions are insane.
Alcohols are no match, and neither are alkanes
Electrophiles hit alkenes, without a lot of pain
Use HBr and HCl to make haloalkanes

But then I get confused as to what we're going to see
Which carbon gets which atom? Call it regiochemistry
I hear there's a brilliant man who gave us clarity
What's his name? What's his name? I have to find the key

Well the word got around, they said "this guys insane, man!"
From the 1800's, a Russian dude they say, man.
Got his education and didn't forget from whence he came, man
The world's got to know his name. What's his name, man?

Vladimir Markovnikov
My name is Vladimir Markovnikov
And there's just one thing I did explain
Which carbon gets, the halogen?

The key to understanding products of hydrohalogenation
Is that a carbocation is formed by the HX protonation
Stabilize the plus charge with overlapping orbitalization
The official term of course, is hyperconjugation

The more stable cation forms of lower energy
The halide ion comes in and reacts there naturally
It's the one with more carbons, that's maybe two or three
So X is on more substituted carbons don't you see

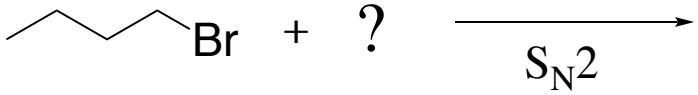
Vladimir Markovnikov
My name is Vladimir Markovnikov
And there's just one thing that I did explain
Which carbon gets, the halogen?

So don't be throwing away my rule
Don't be throwing away my rule
Hey yo, its not that convoluted
Halogen on the carbon that's more substituted
So don't be throwing away my rule

Vladimir Markovnikov
My name is Vladimir Markovnikov
And there's just one thing I did explain
Which carbon gets, the halogen.

So don't be throwing away my rule
Don't be throwing away my rule
Hey yo, its not that convoluted
Halogen on the carbon that's more substituted
So don't be throwing away my rule

Shape of S_N2



The club ain't the best place to find nucleophiles
So the lab is where I go
Me and my friends in solvent
Moving fast but reacting slow
Come over and start up a reaction with just me
And trust me I'll give it a chance now
Let's react, stop, put your charge over here
And then we start to react, and now I'm singing like
You know I want to make a bond
Your charge was handmade for a reagent like me
Come on now, follow my lead
I'm an electrophile, don't mind me
Say now let's not talk too much
Get through solvent and put your electrons on me
Come on now, follow my lead,
Come, come on now, follow my lead

I'm attracted to the charge of you
We push and pull like charges do
Although my orbitals are reacting too
Come on let's get bonding
Transition state is coming true
Time to finish the S_N2
Creating a bond brand new
Come on let's get bonding
Oh-I-oh-I-oh-I-oh-I-oh-I
Come on let's get bonding
Oh-I-oh-I-oh-I-oh-I-oh-I
Come on let's get bonding
Oh-I-oh-I-oh-I-oh-I-oh-I
Come on let's get bonding
We need to make a bond brand new
Come on now let's S_N2.

" Don't Stop, Believin'

Just a Houston girl,
Living in a Longhorn world.
She took the premed train
Straight to OChem 1

Just a Plano boy,
Born and raised in full burnt orange,
He took the premed train
Straight to OChem 1

They study in a smoky room,
Smell of vapes and Mountain Dew
For an A they study all night
It goes on and on and on and on

Alkanes to alkynes
Up and down the I-35
Two students studying in the night
Roadmaps, reactions
Living just to pass the final
Will they ever get it right

Working hard to get my grade
Everybody wants an "A"
Trying anything to ace this class
Just one more exam
Some will win, some will lose
I don't want to sing the blues
OChem never seems to end
It goes on and on and on and on

Alkanes to alkynes
Up and down the I-35
Two students studying in the night
Roadmaps, reactions
Living just to pass the final
Will they ever get it right

Don't stop believin'
Hold on to that "A" feelin'
Roadmaps, reactions
Ohohohohohoh

Don't stop believin'
Hold on
Roadmaps, reactions
Ohohohohohoh

Don't stop believin'
Hold on to that "A" feelin'
Roadmaps, reactions
Ohohohohohoh

We All Love Organic Chemistry

In the town where I was born,
Lived a man of chemistry.
And he told us of his life
In the organic laboratory.

Making molecules to fight disease
Coming up with their syntheses.
So we sit in 320M
Learning organic chemistry.

Refrain:
We all love organic chemistry
Synthetic chemistry
Molecules with "C"
We all love organic chemistry
Synthetic chemistry
Molecules with "C"

All our friends think we're a bore
Our grade point averages begin with 4.
But we await graduation day
To work in lab for meager pay.

But its OK, who else can say
They're curing cancer or fighting AIDS.
We hope that you in 320M
Respect organic chemistry

Refrain:
We all love organic chemistry
Synthetic chemistry
Molecules with "C"
We all love organic chemistry
Synthetic chemistry
Molecules with "C