

Multidimensional NMR Experiments

Chem 8361/4361:
Interpretation of Organic Spectra

2D NMR Spectroscopy

General Information

- More complicated experiments to set up than ^1H and ^{13}C
- Changes in pulses (#, length, angles, mixing times, etc.)
- Observe effects based on relationship of nuclei
 - **Can be homonuclear (same nuclei) (e.g. H–H) or heteronuclear (different nuclei) (e.g. H–C, H–P, etc.)**
- Will only go over the what the experiments tell you and how to interpret, and only for the most common and widely used for solving organic structures
 - DEPT, H–H COSY, HMQC (HETCOR), HMBC, INADEQUATE (C–C COSY)
- There is a whole alphabet soup of other experiments (both 1D and 2D)
 - EXSY, TOCSY, HOHAHA, INEPT, WATERGATE, and many more

2D NMR Spectroscopy

Number of Protons on Carbon

DEPT (*D*istortionless *E*nhancement by *P*olarisation *T*ransfer)

- Used to be known as APT (Attached Proton Test)
 - DEPT is ^1H -detected; APT is ^{13}C -detected
- Tells you how many protons are attached to a particular carbon
 - negative peaks = CH_2
 - positive peaks = CH and CH_3 (distinguishable with further processing)
 - “missing” peaks = carbons w/o protons
- With a little help from IR and chemical shift of ^1H and ^{13}C , can get a rough idea of molecular weight

2D NMR Spectroscopy

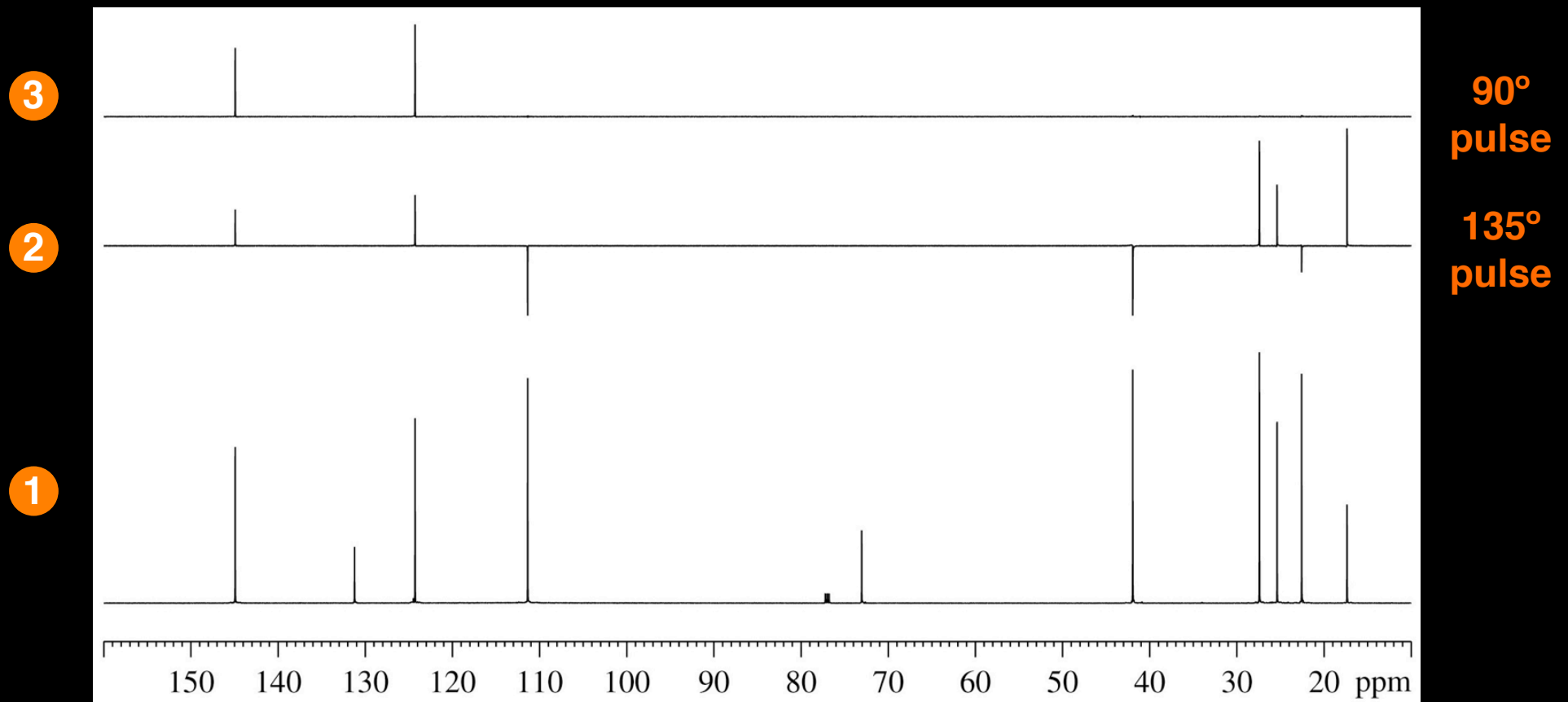
Number of Protons on Carbon

DEPT (Distortionless Enhancement by Polarisation Transfer)

1 = Carbon spectrum

2 = \downarrow CH₂
 \uparrow CH, CH₃

3 = \uparrow CH

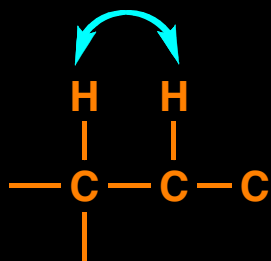


2D NMR Spectroscopy

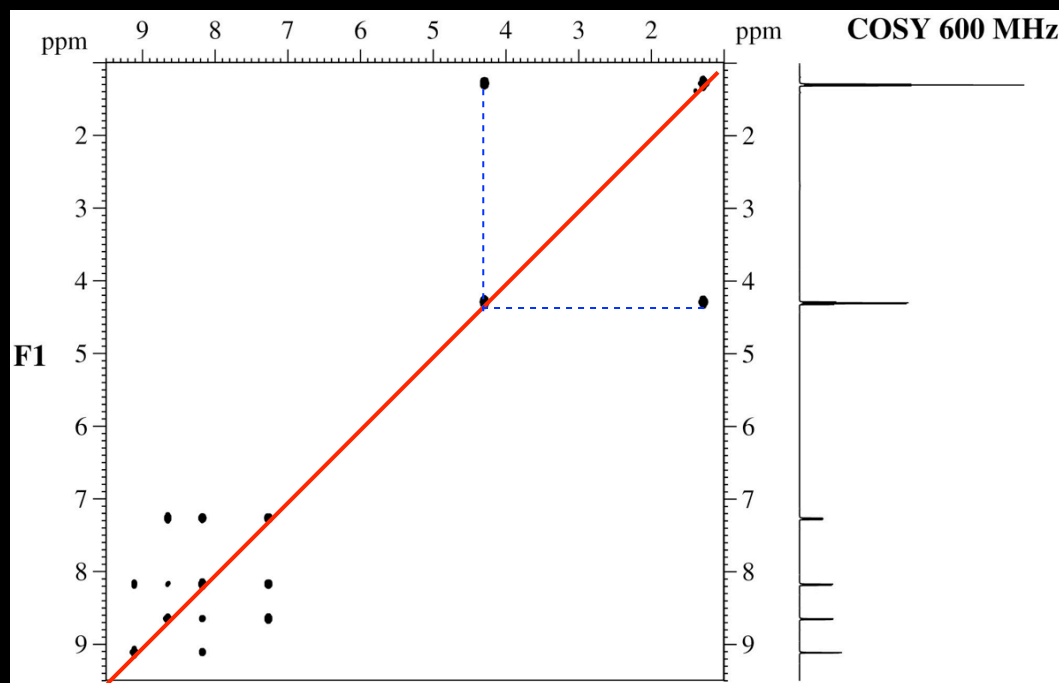
Who is Talking to Who?

^1H - ^1H COSY (Correlation Spectroscopy)

- Tells you which protons are coupled to one another
- Very useful when peaks are overlapping in ^1H NMR and you are unable to calculate coupling constants, or when there are a lot of similar coupling constants
- Cross peaks are coupled to each other



1 bond H-H coupling



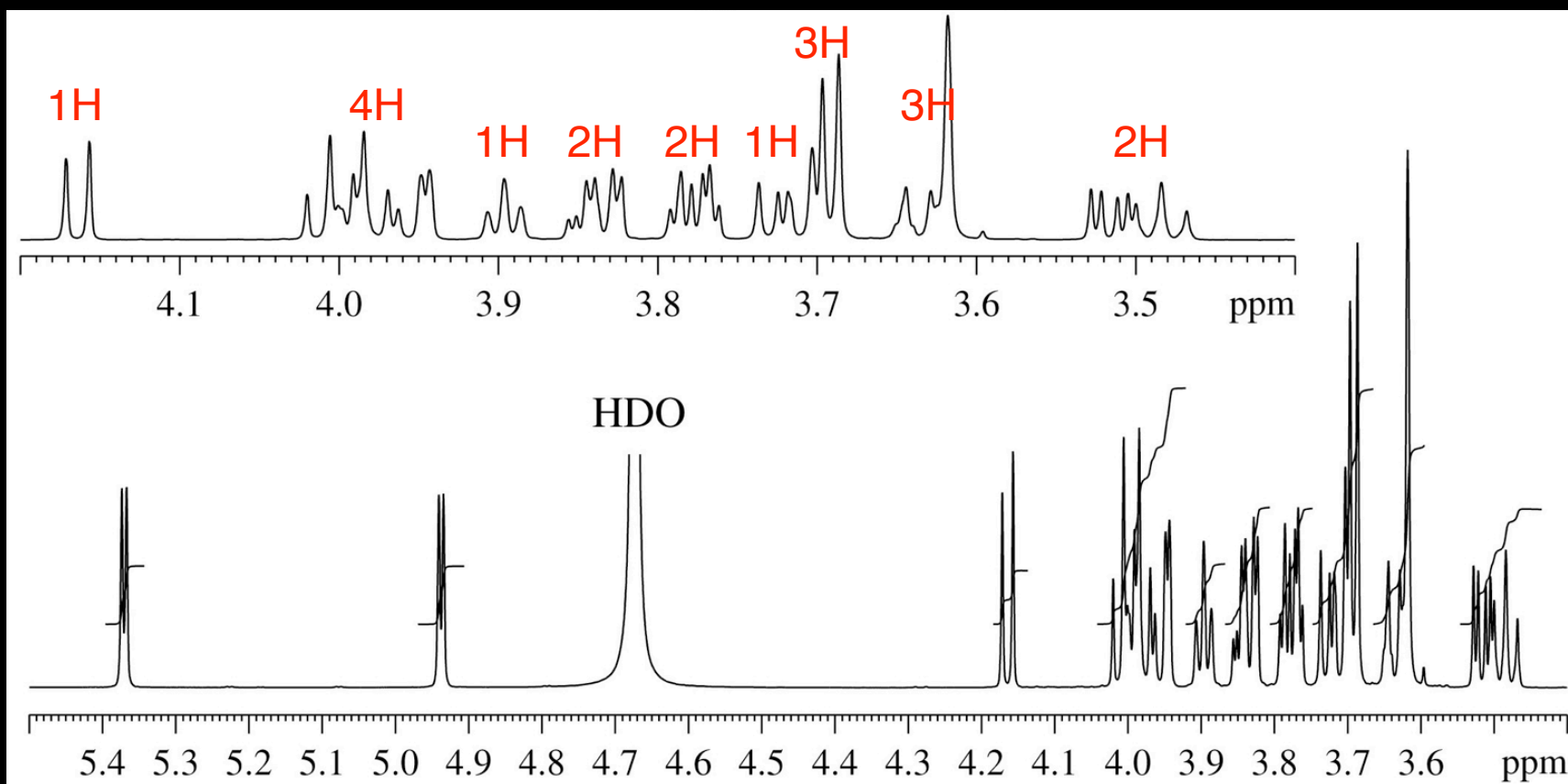
- Newer method is DQF (Double Quantum Filtered)-COSY
 - same information, but looks “cleaner”

2D NMR Spectroscopy

Who is Talking to Who?

^1H - ^1H COSY (Correlation Spectroscopy)

- Overlapping protons and a lot of similar coupling constants

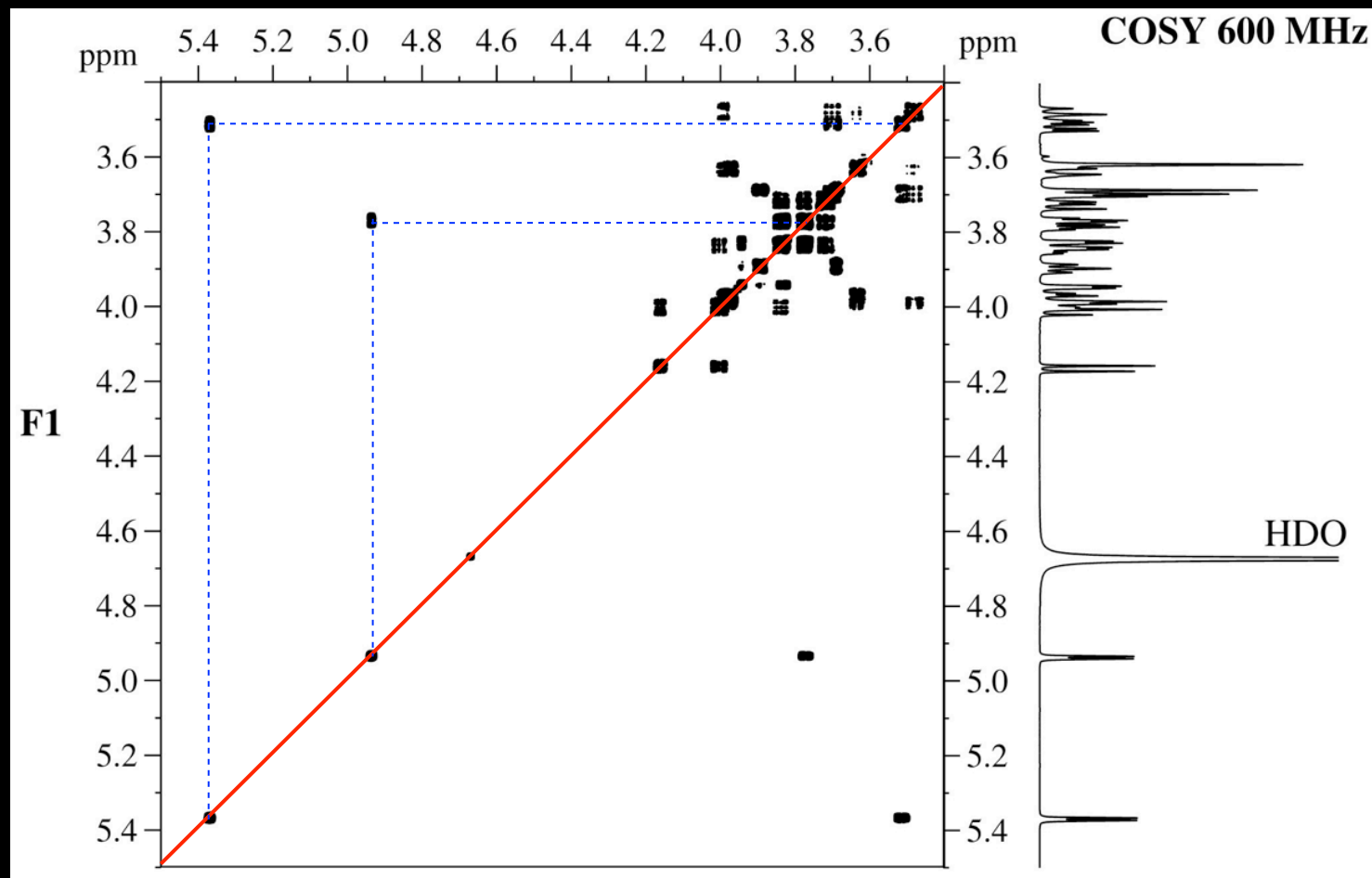


Raffinose—a trisaccharide

2D NMR Spectroscopy

Who is Talking to Who?

^1H - ^1H COSY (Correlation Spectroscopy)

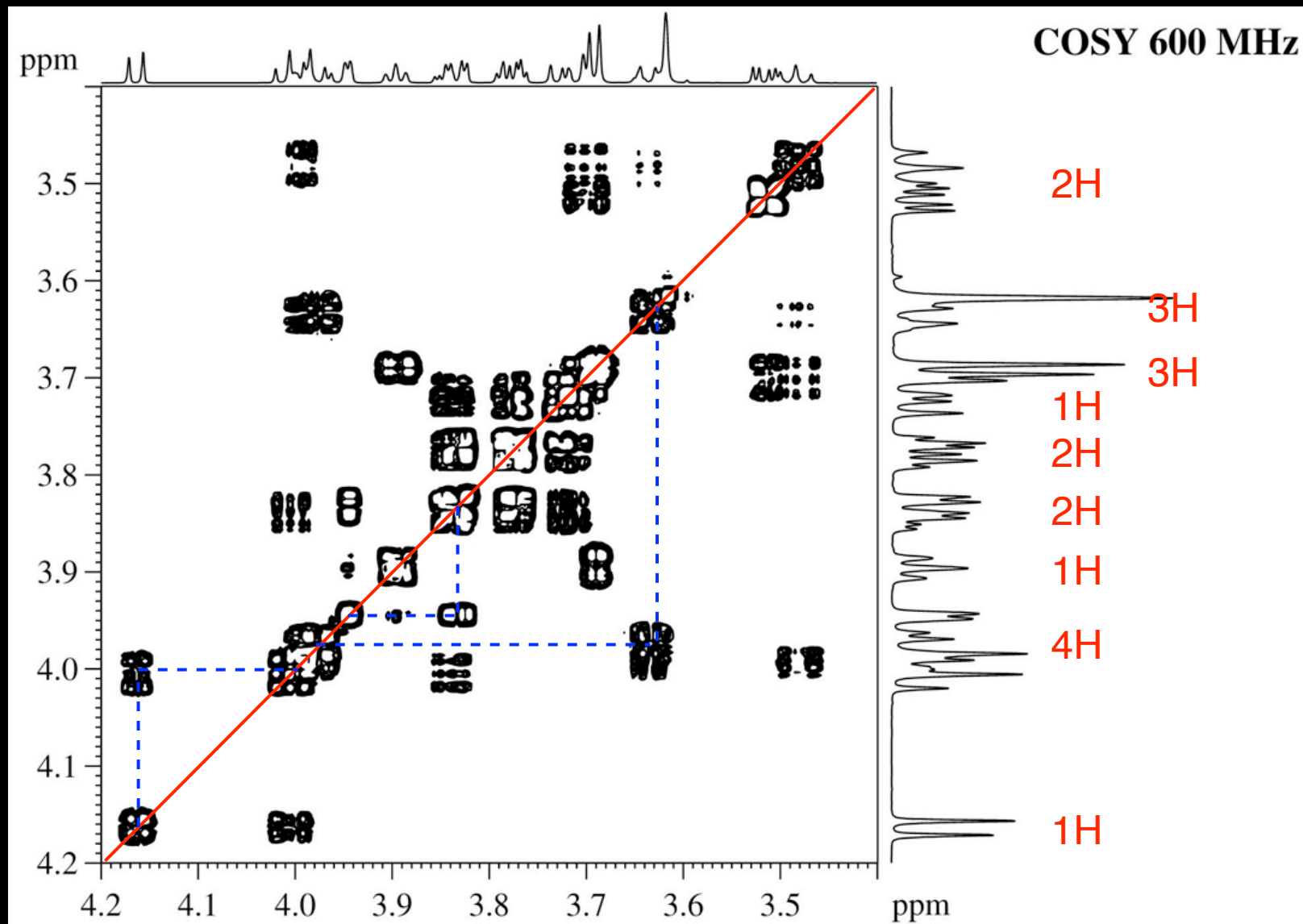


Raffinose—a trisaccharide

2D NMR Spectroscopy

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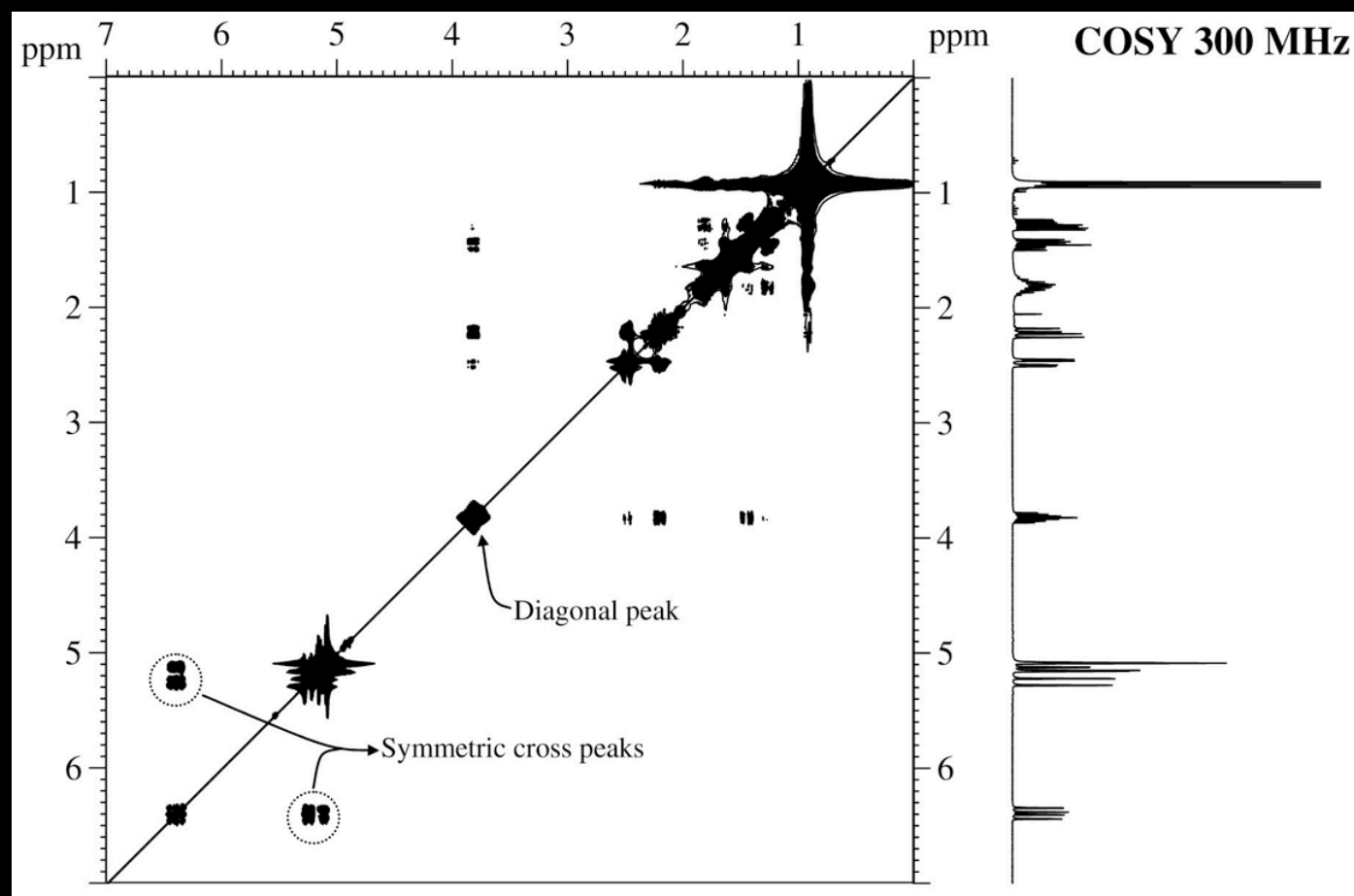
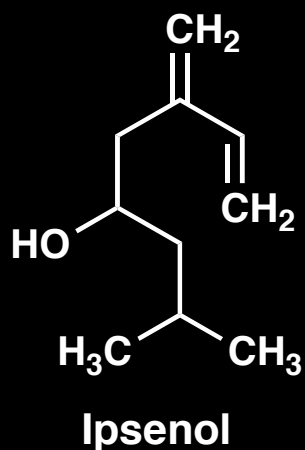


2D NMR Spectroscopy

Who is Talking to Who?

^1H - ^1H COSY (Correlation Spectroscopy)

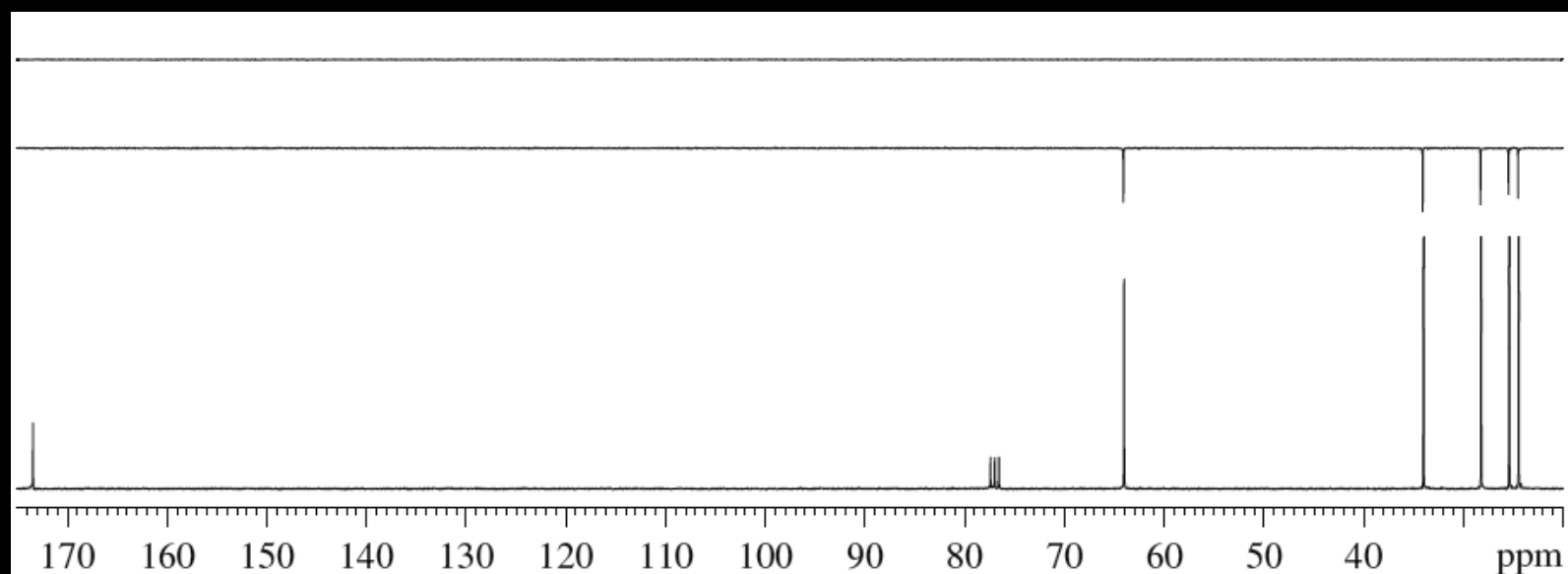
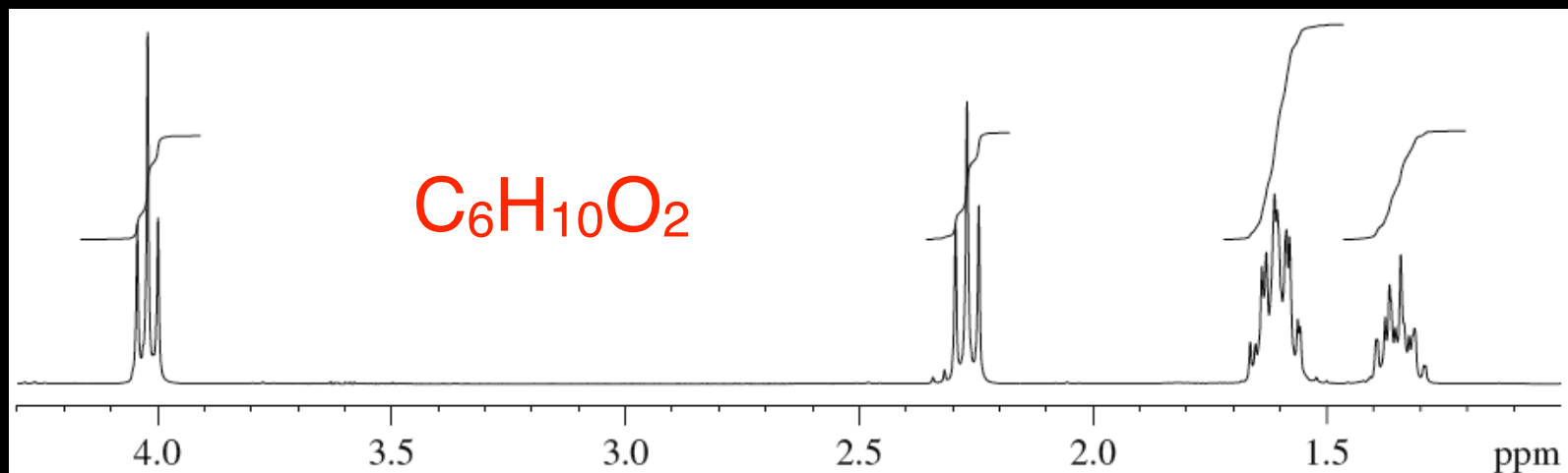
– DQF-COSY: *Double Quantum Filtered COSY* – cleans up the spectrum by reducing noncoupled systems (e.g. CH_3 singlets)



2D NMR Spectroscopy

Who is Talking to Who?

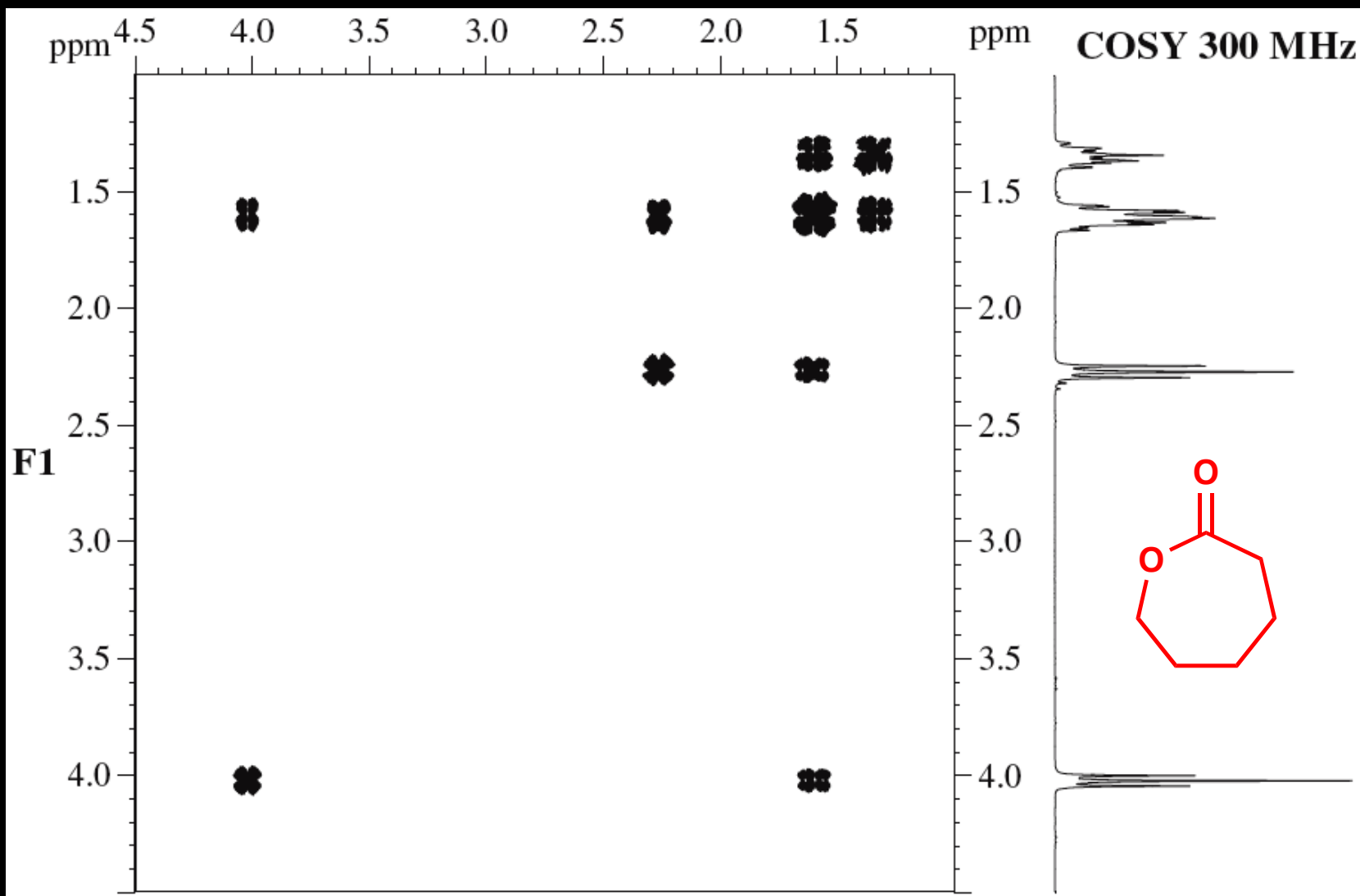
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2D NMR Spectroscopy

Who is Talking to Who?

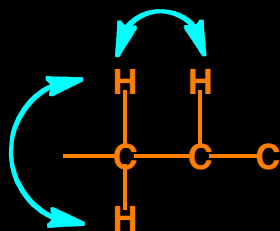
^1H - ^1H COSY (Correlation Spectroscopy)



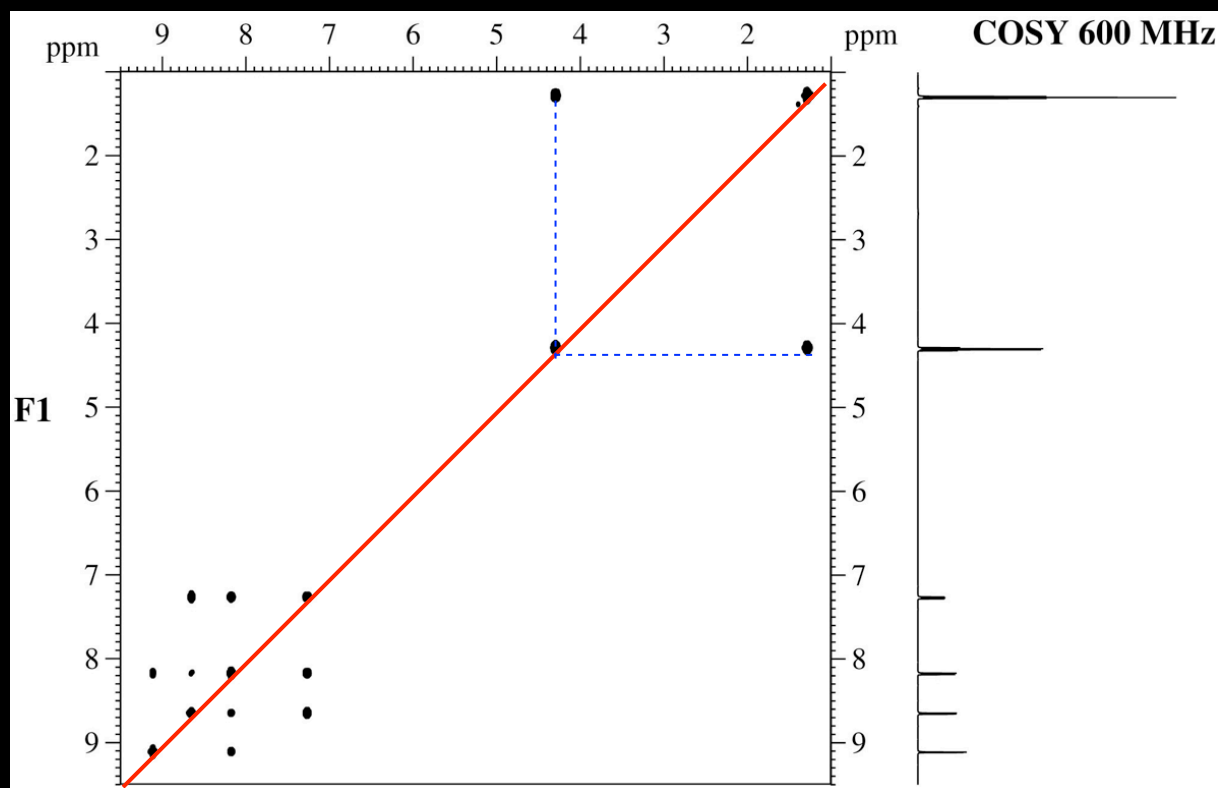
Recall...

^1H - ^1H COSY

- Tells you which protons are coupled to one another
- Very useful when peaks are overlapping in ^1H NMR and you are unable to calculate coupling constants, or when there are a lot of similar coupling constants
- Cross peaks are coupled to each other



2 & 3 bond H-H coupling



Recall...

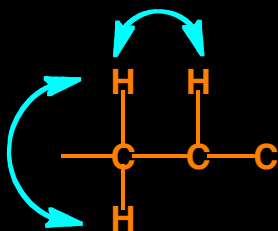
^1H - ^1H COSY

This can still cause ambiguities!

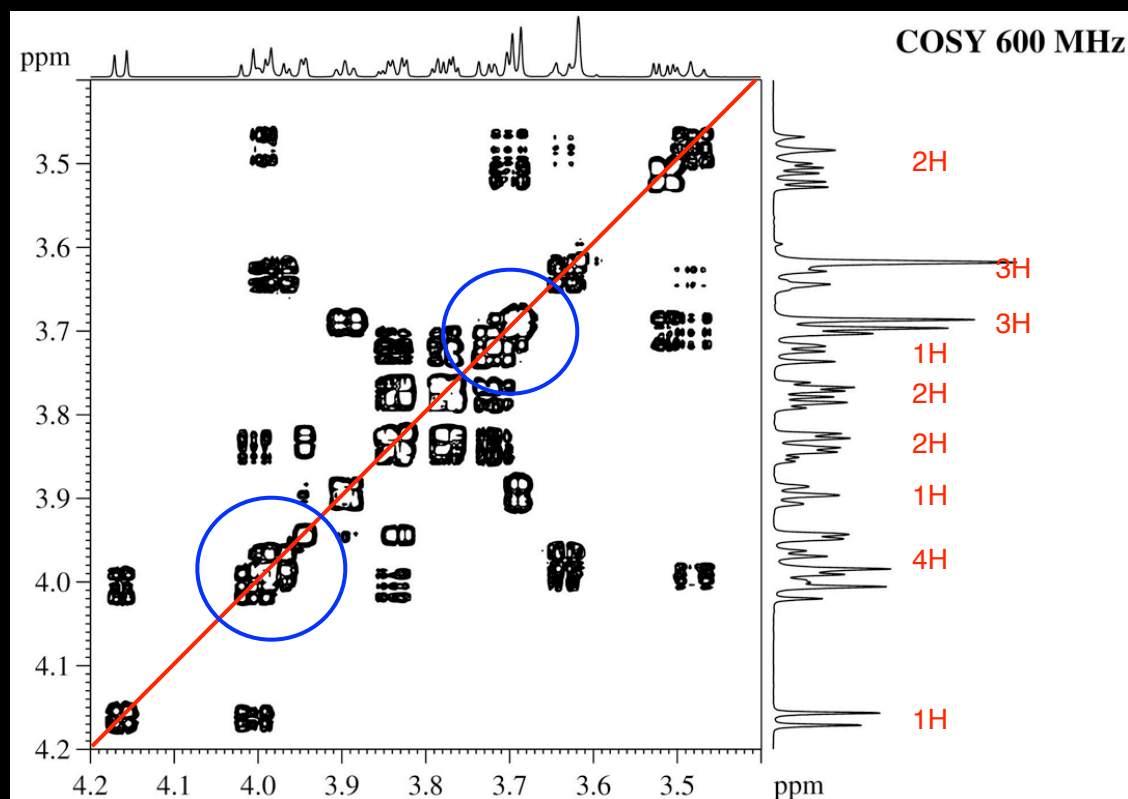
– Tells you which protons are coupled to one another

– Very useful when peaks are overlapping in ^1H NMR and you are unable to calculate coupling constants, or when there are a lot of similar coupling constants

– Cross peaks are coupled to each other



2 & 3 bond H-H coupling

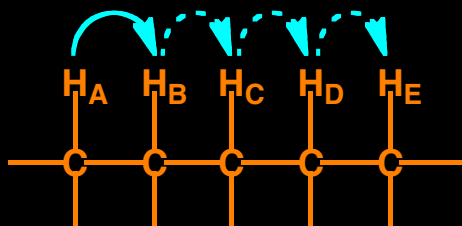


2D NMR Spectroscopy

Who is Talking to Who?

^1H - ^1H TOCSY (Total Correlation Spectroscopy)

- Tells you which protons are in the same spin system (a continuous chain of spin-spin coupled protons)
- Magnetization from H_A is transferred to H_B , which then transfers to H_C and on down the line



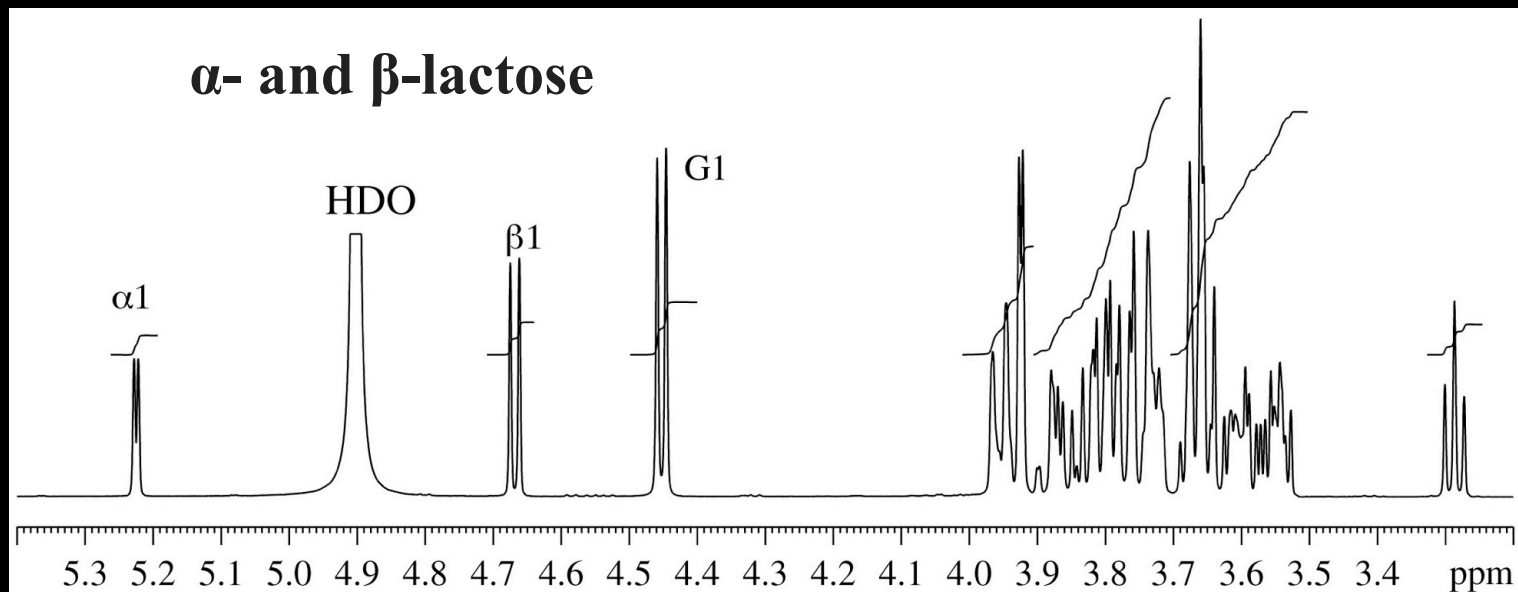
- Can be run as either a 1D or 2D experiment
- Running as a 1D experiment greatly simplifies spectra with severe signal overlap
- Related experiment (HOHAHA) gives essentially the same information
- Can also observe one-bond ^1H - ^{13}C couplings (HMQC-TOCSY, hetero-TOCSY, HEHAHA) - will not discuss

1D TOCSY

Spin System Identification

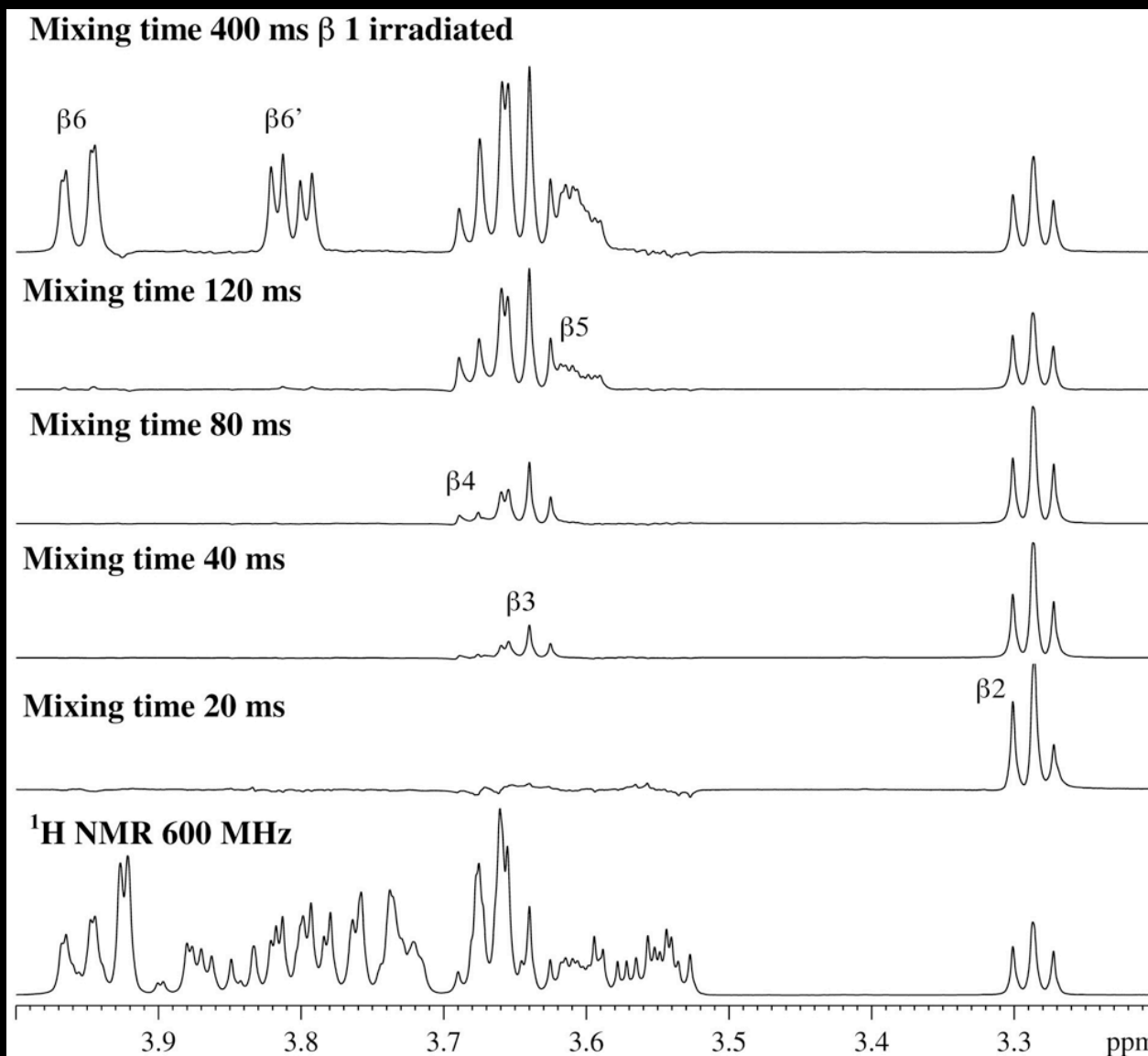
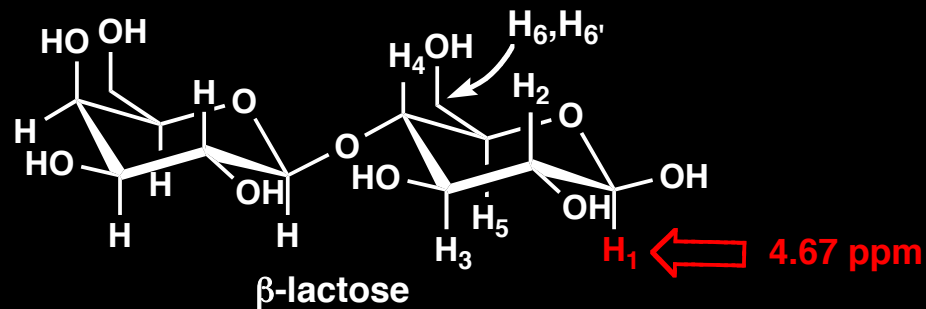
^1H - ^1H TOCSY (Total Correlation Spectroscopy)

- Irradiate at frequency of proton of interest
- Wait a period of time (typically 20 to 400 ms) and then collect 1D spectrum
- Only observe protons to which magnetization has been transferred
- Short periods of time (20 ms) will only give rise to “single step” transfers; longer periods of time allow magnetization to propagate further

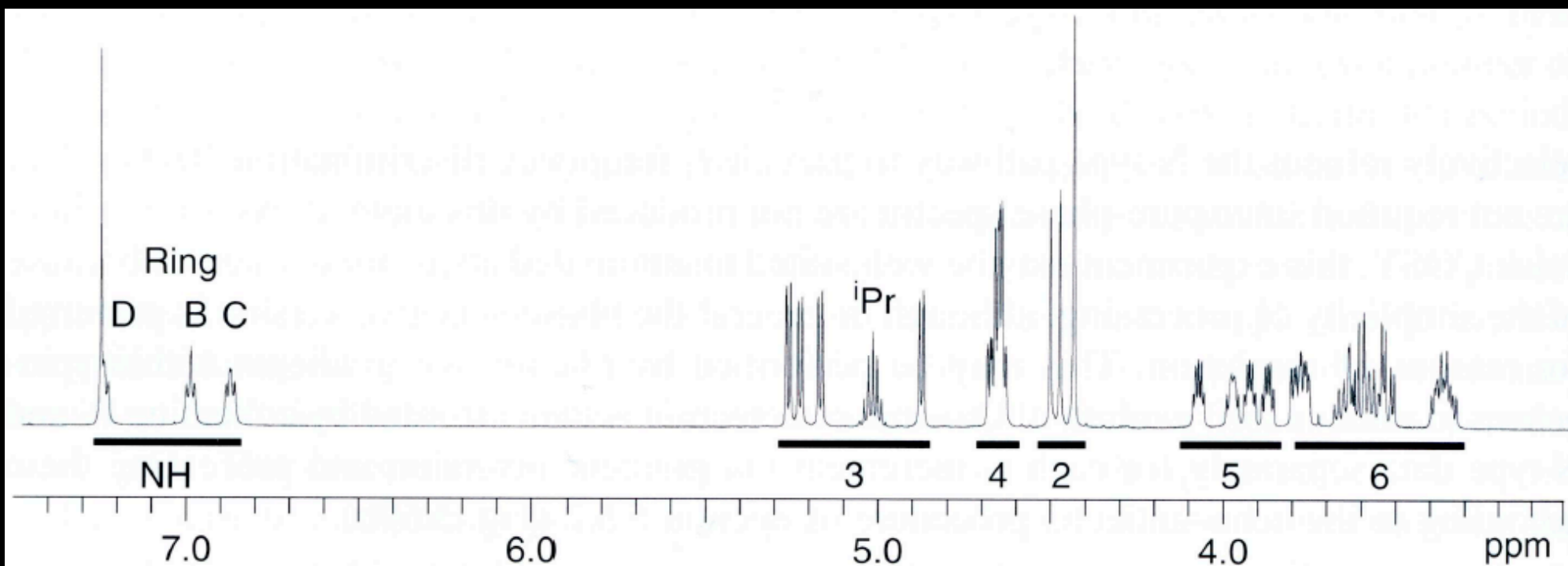
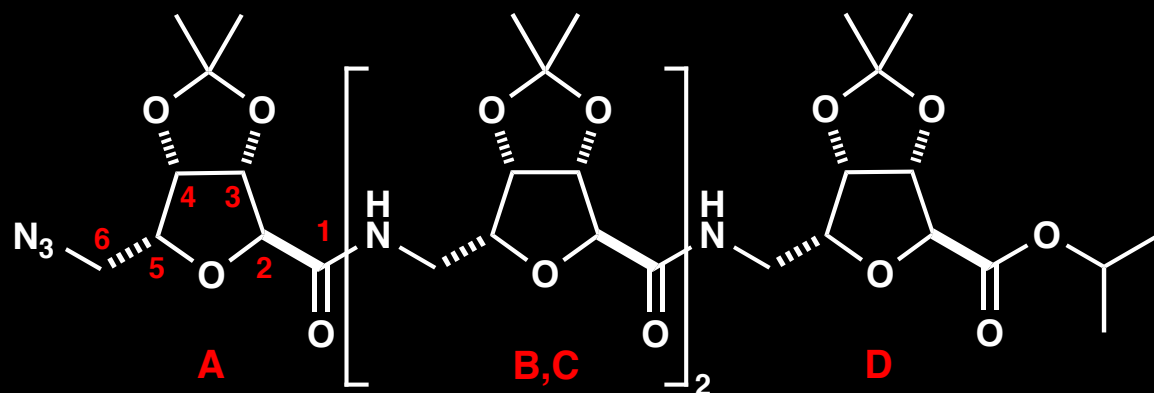


1D TOCSY

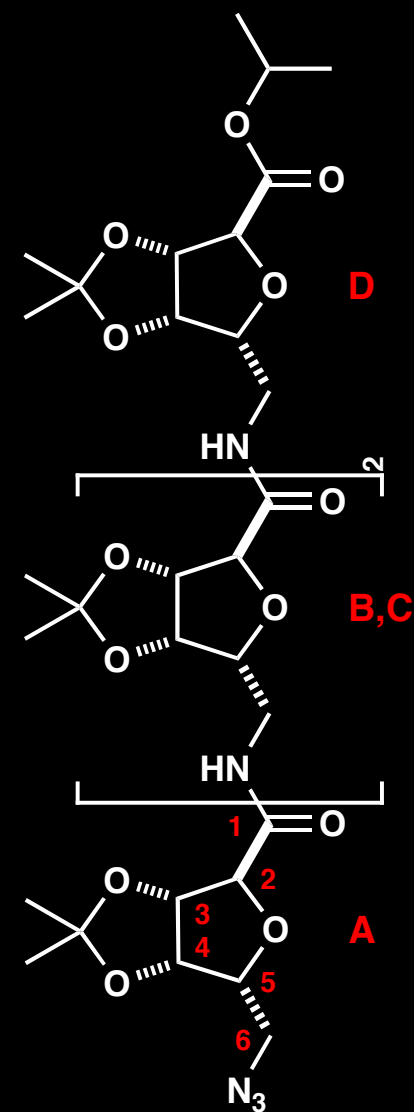
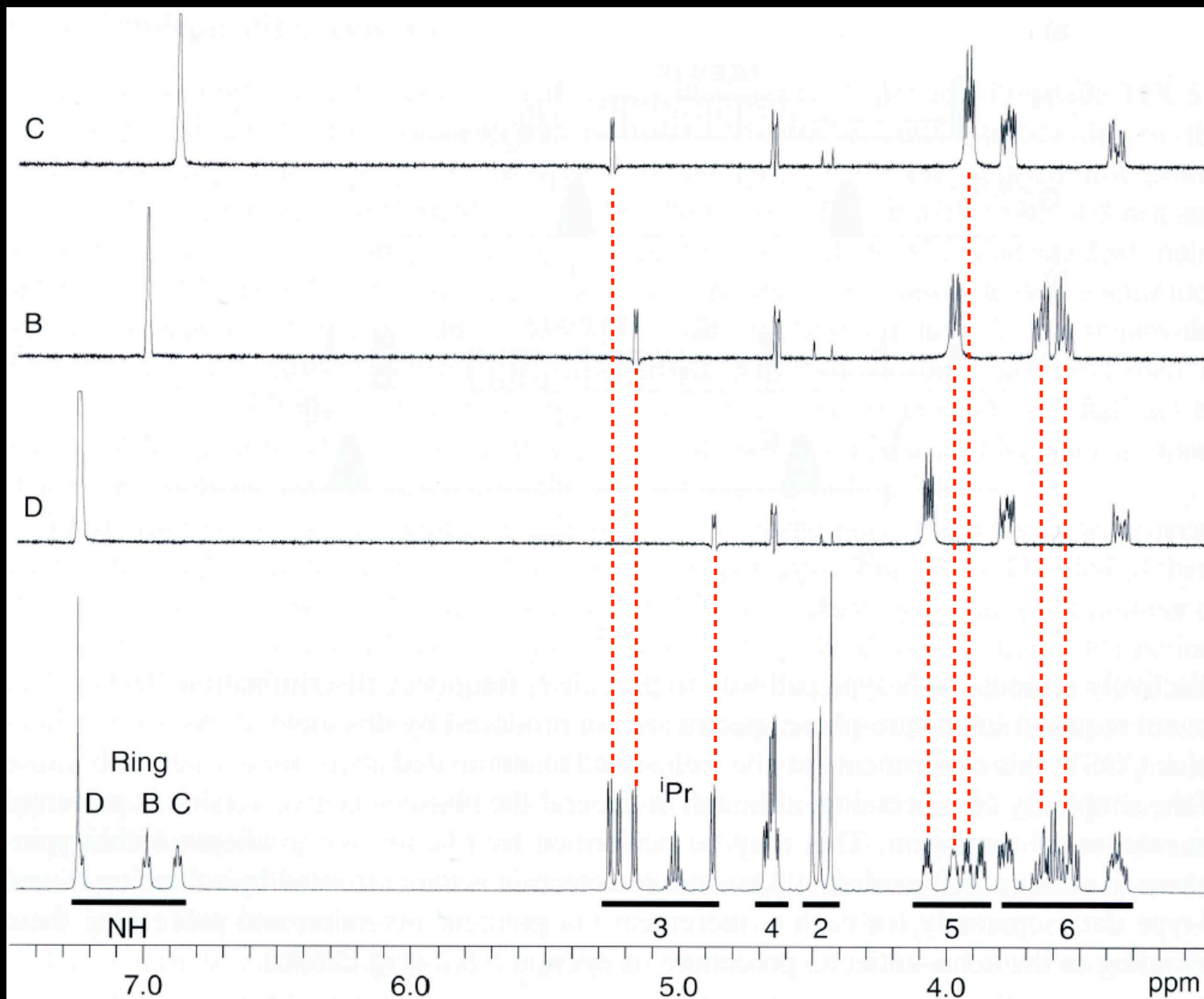
Spin System Identification



1D TOCSY



1D TOCSY

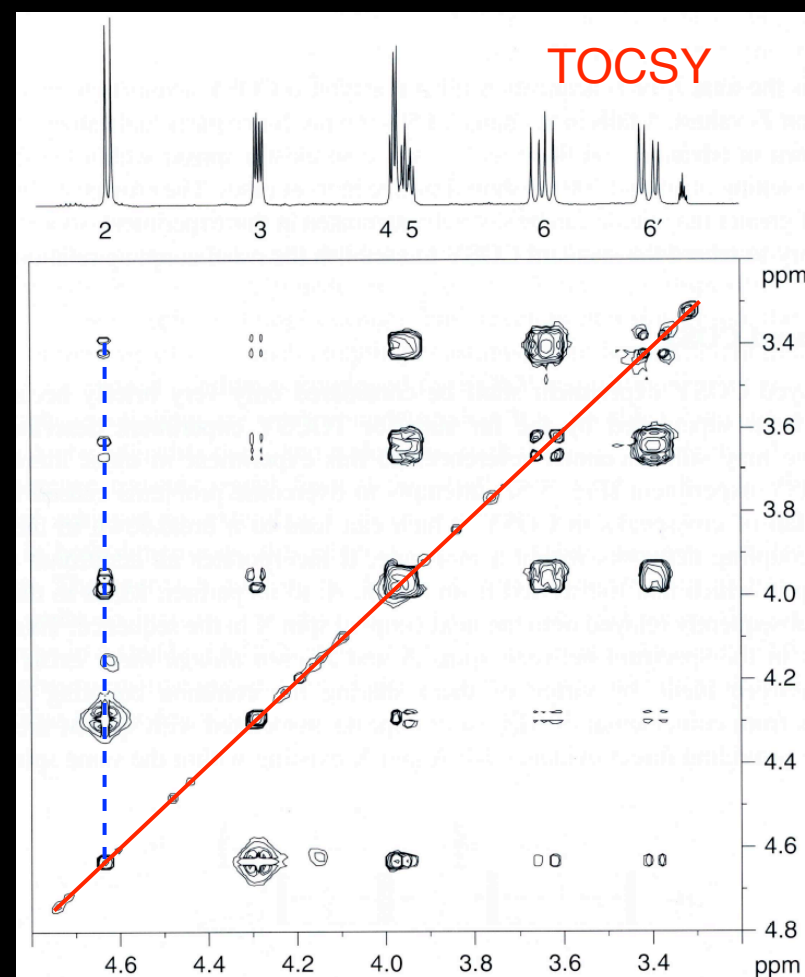
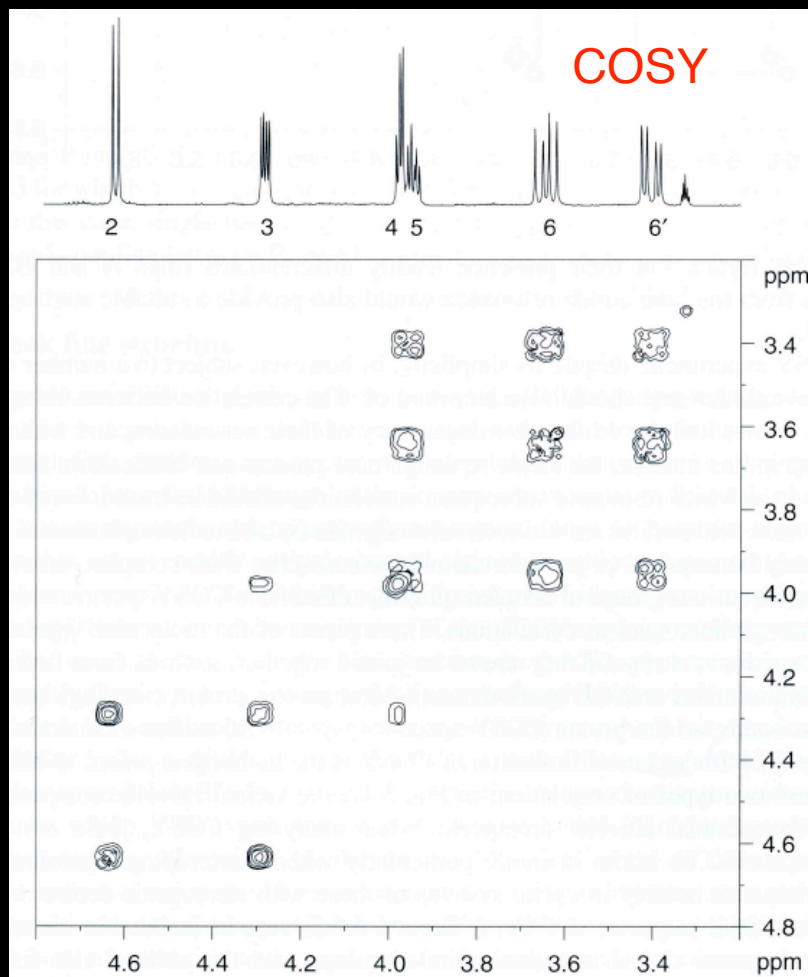
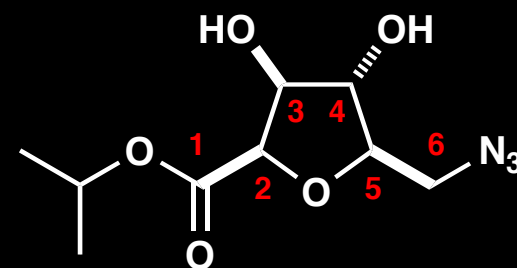


2D TOCSY

Spin System Identification

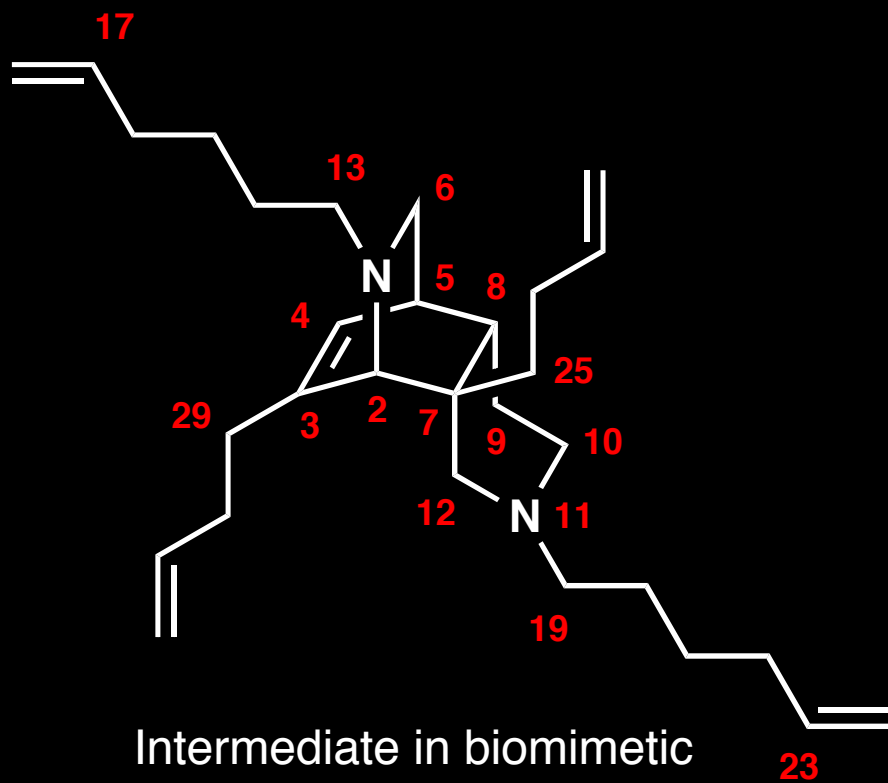
^1H - ^1H TOCSY (Total Correlation Spectroscopy)

– Cross peaks are in the same spin system

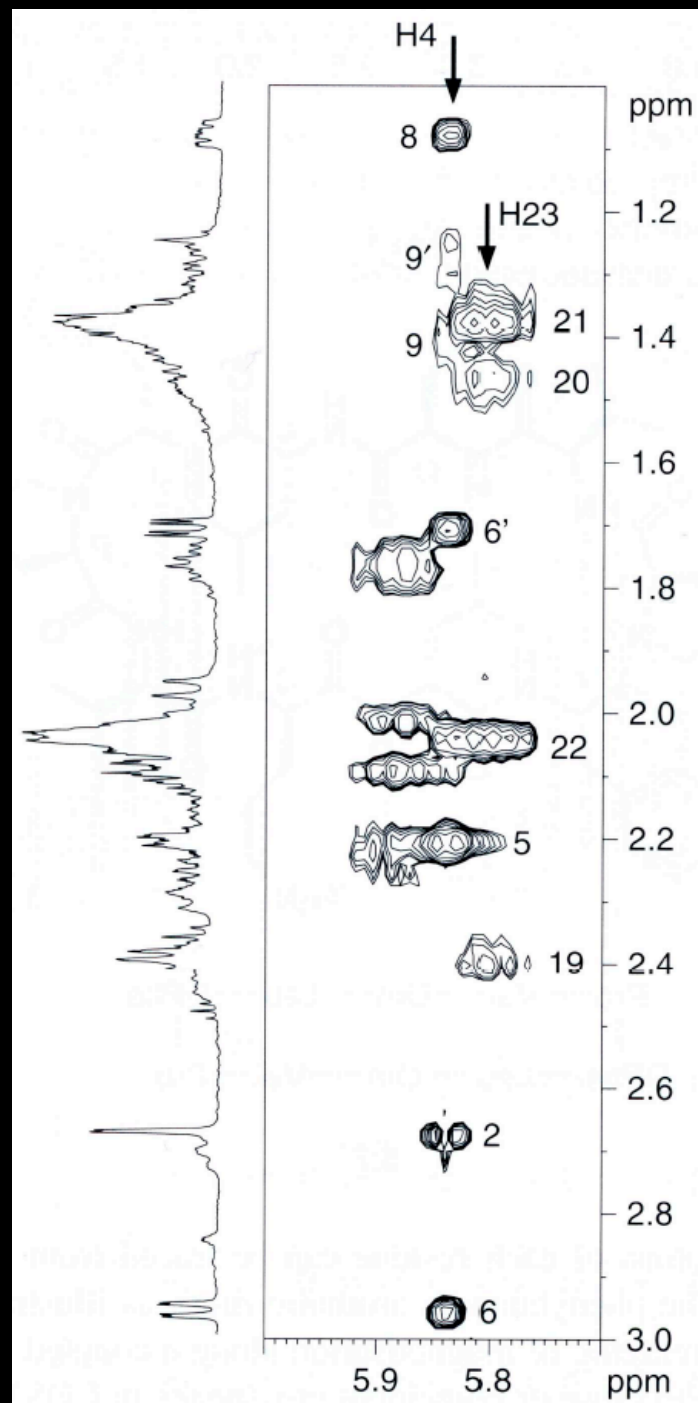


2D TOCSY

– Cross peaks are in the same spin system

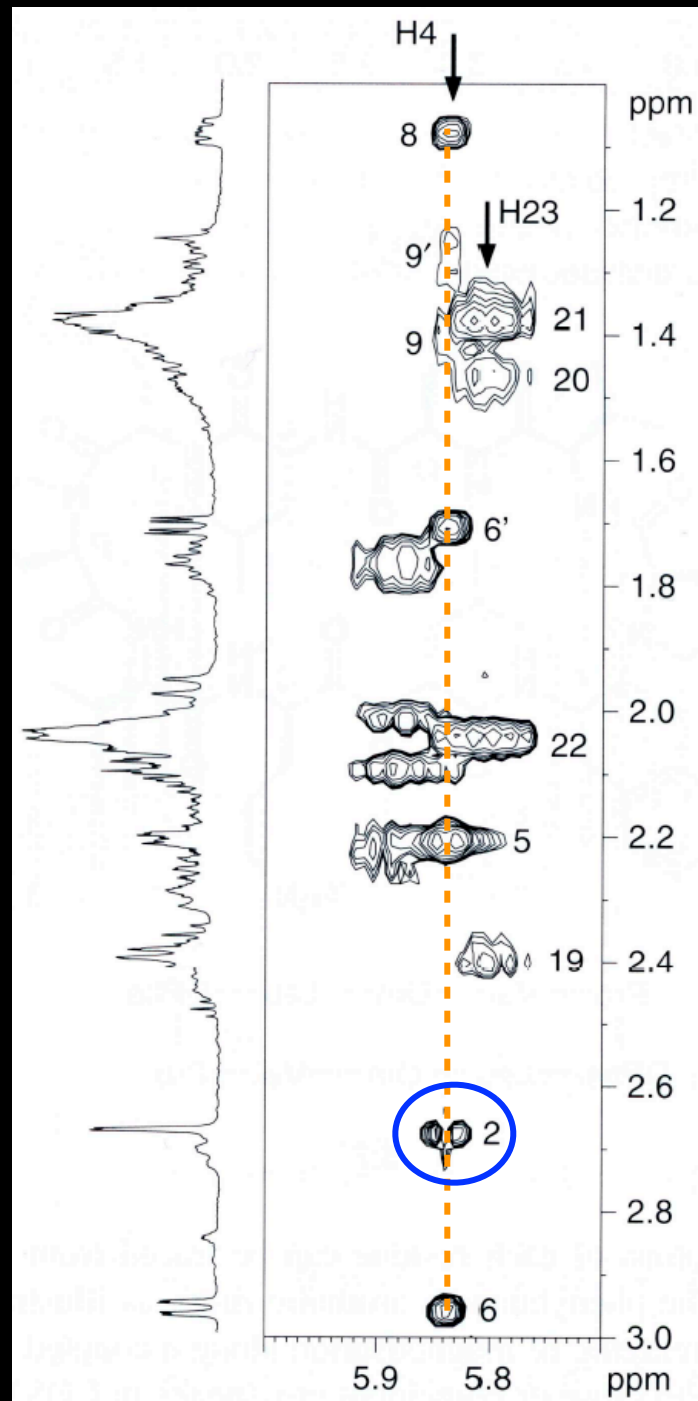
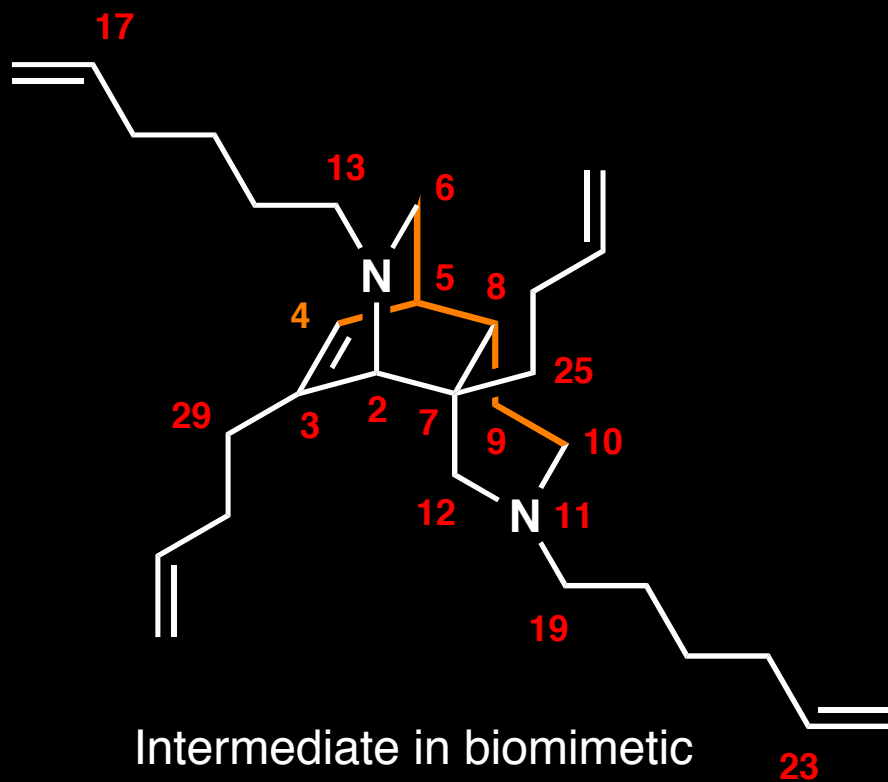


Intermediate in biomimetic synthesis of manzamine



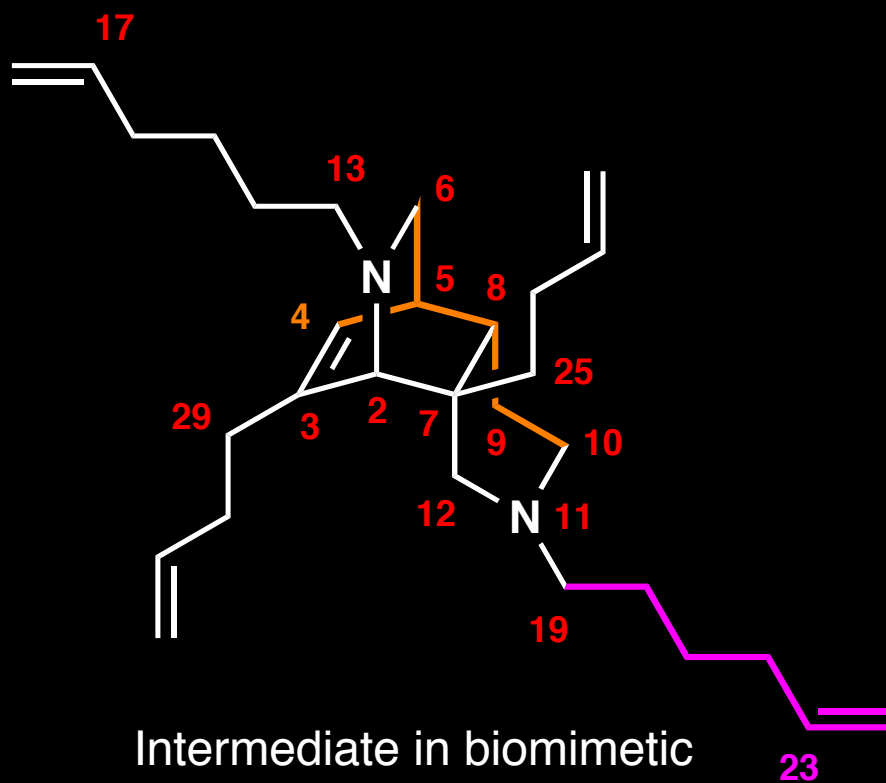
2D TOCSY

– Cross peaks are in the same spin system

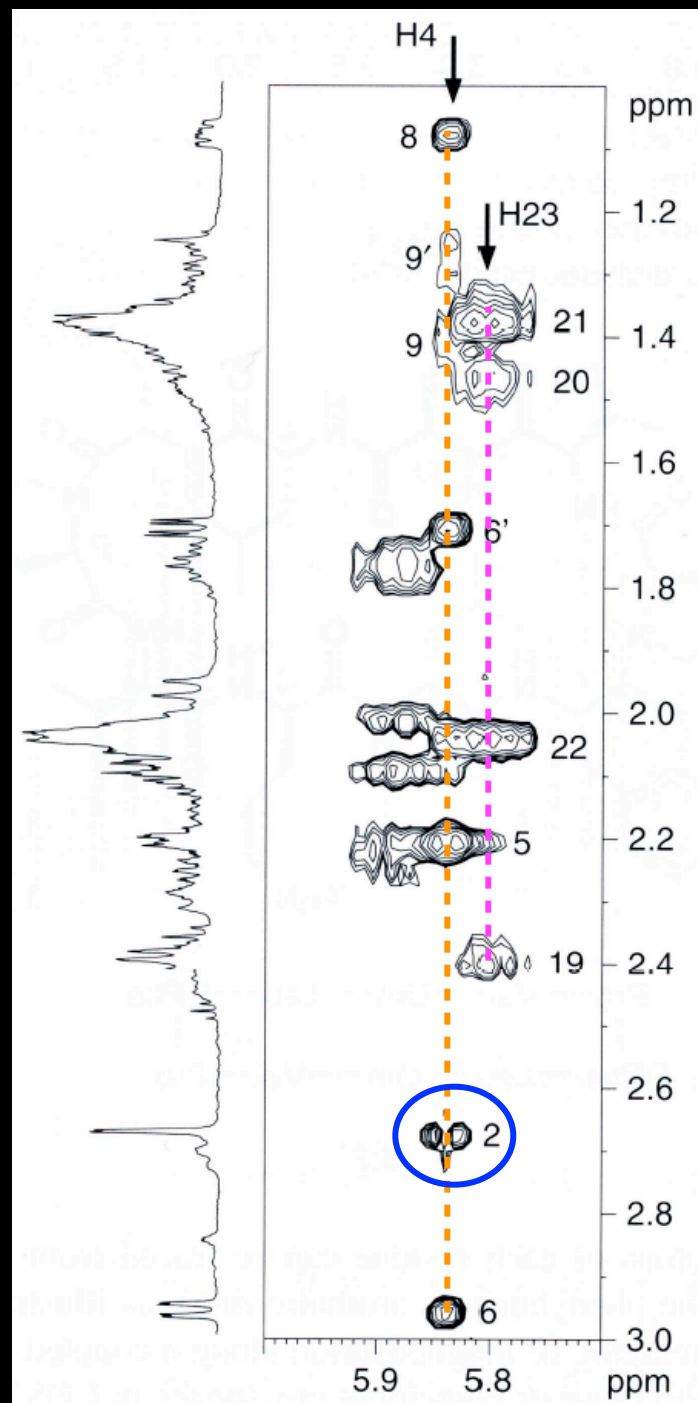


2D TOCSY

– Cross peaks are in the same spin system



Intermediate in biomimetic synthesis of manzamine

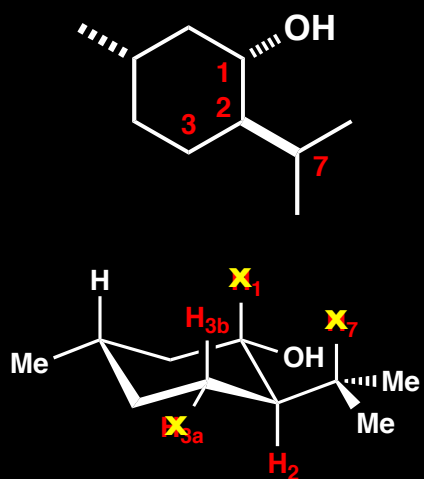


New Developments

Deconvolution via MDEC

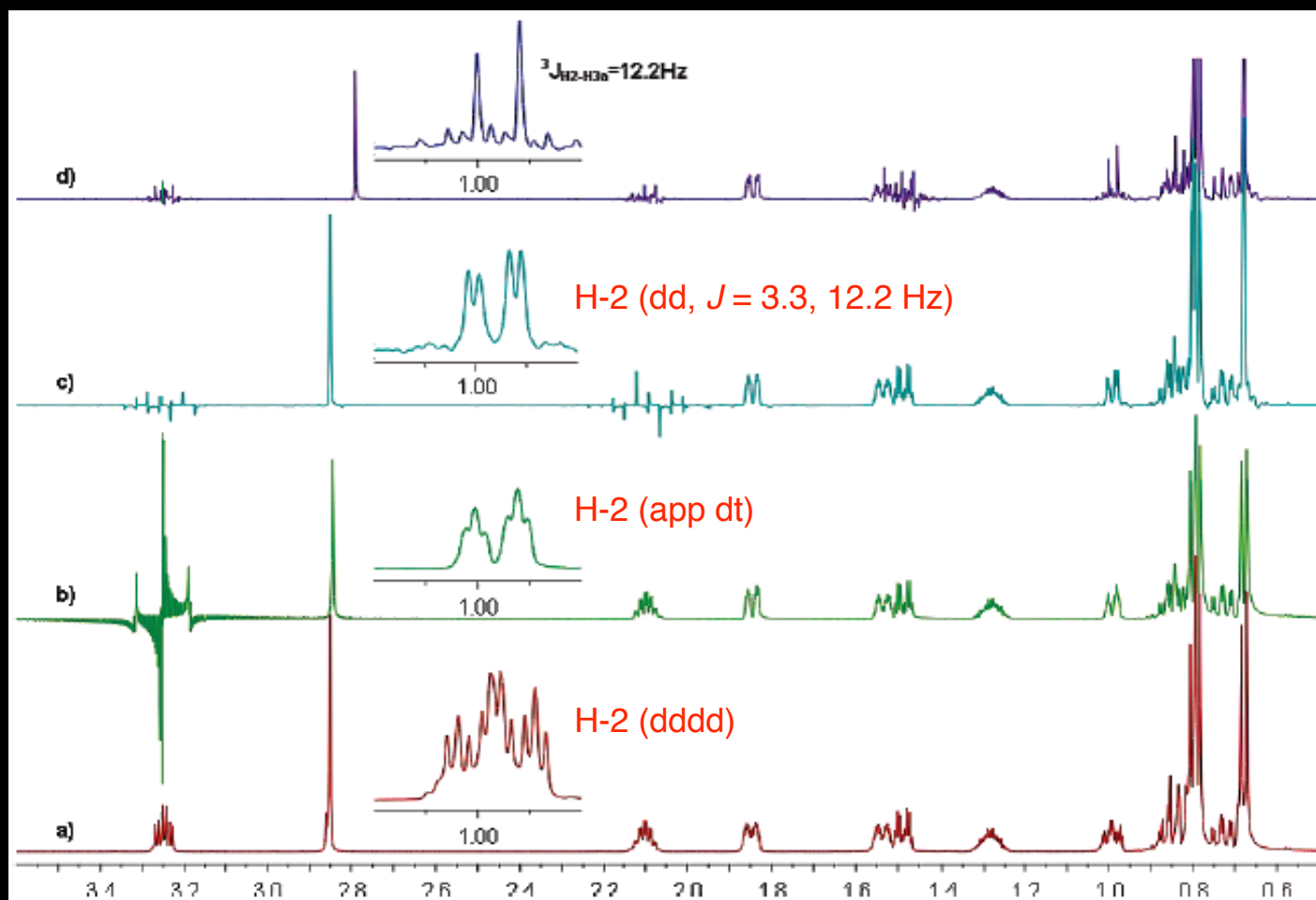
MDEC (Multi Frequency Homonuclear Decoupling)

- Conceptually the same as the homonuclear decoupling experiment mentioned earlier, but allows multiple frequencies to be decoupled *at the same time*



- (a) ¹H NMR
- (b) irr @ H-1
- (c) irr @ H-1/H-7
- (d) irr @ H-1/H-3a/H-7

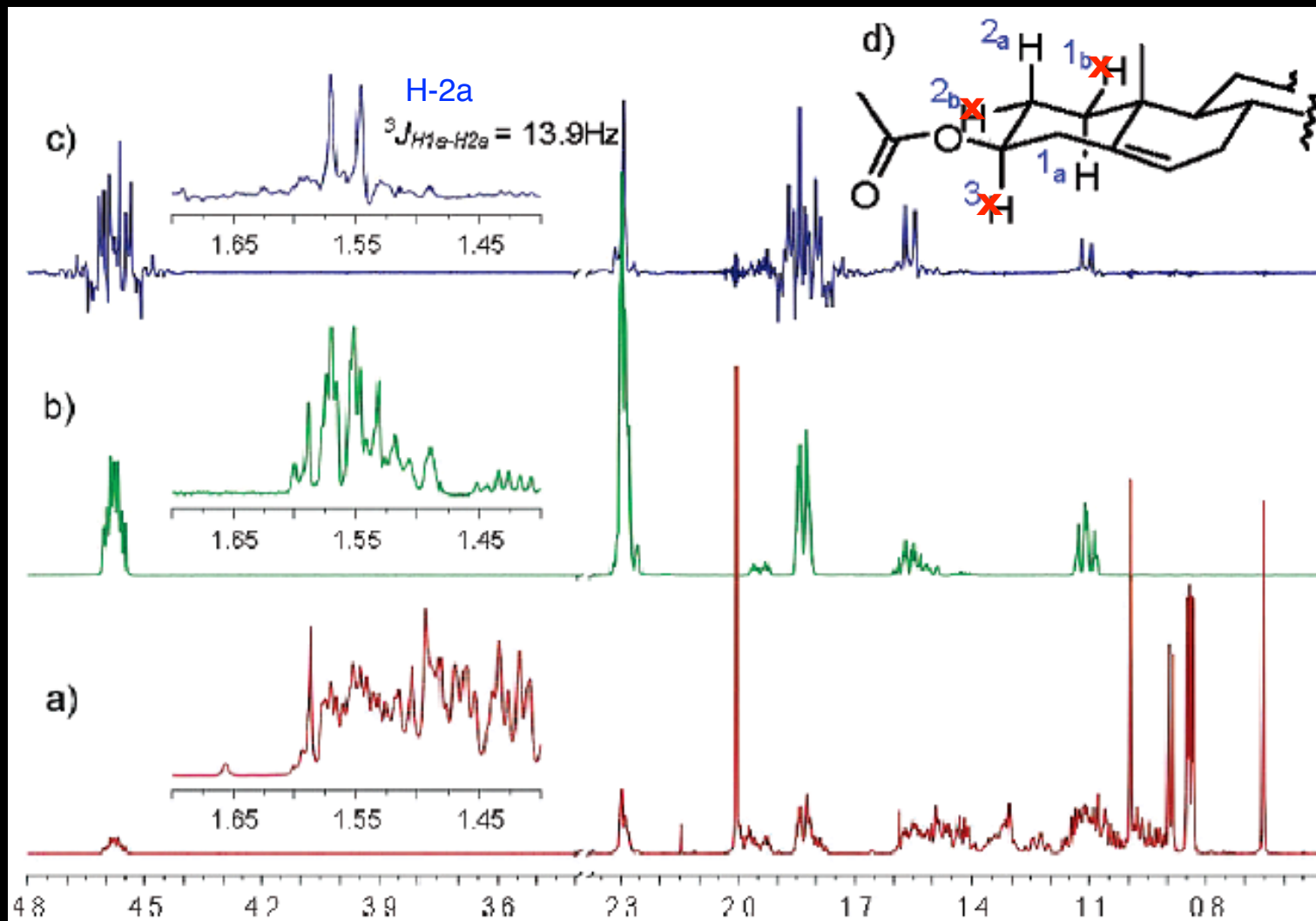
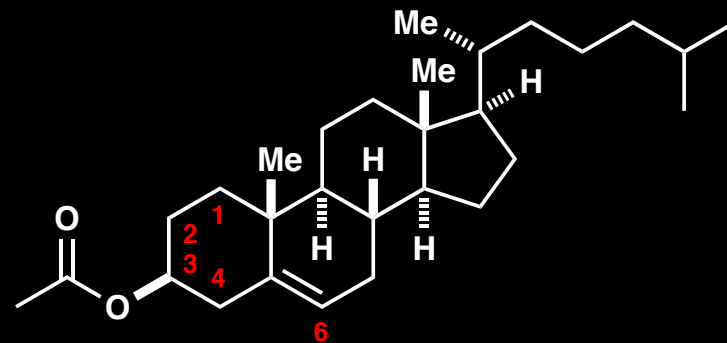
J. Am. Chem. Soc. **2009**, *131*,
15994–15995



New Developments

Deconvolution via MDEC

1D-TOCSY-MDEC



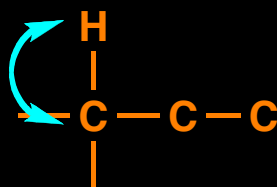
- (a) ^1H NMR
- (b) 1D-TOCSY
irr @ H-3
- (c) 1D-TOCSY
irr @ H-3 with
MDEC @ H-1b,
H-2b, H-3

2D NMR Spectroscopy

Who is Talking to Who?

^1H - ^{13}C COSY

- HETCOR (Heteronuclear Correlation)
 - older experiment; ^{13}C -detected
- HMQC (Heteronuclear Multiple Quantum Correlation) and HSQC (Heteronuclear Single Quantum Correlation)
 - newer experiments; ^1H -detected; largely replaced HETCOR
- Both give same information, experimentally very different
- Peaks have one-bond coupling (i.e. attached directly)
- Compliments DEPT
- Particularly useful for diastereotopic protons

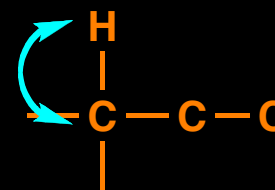
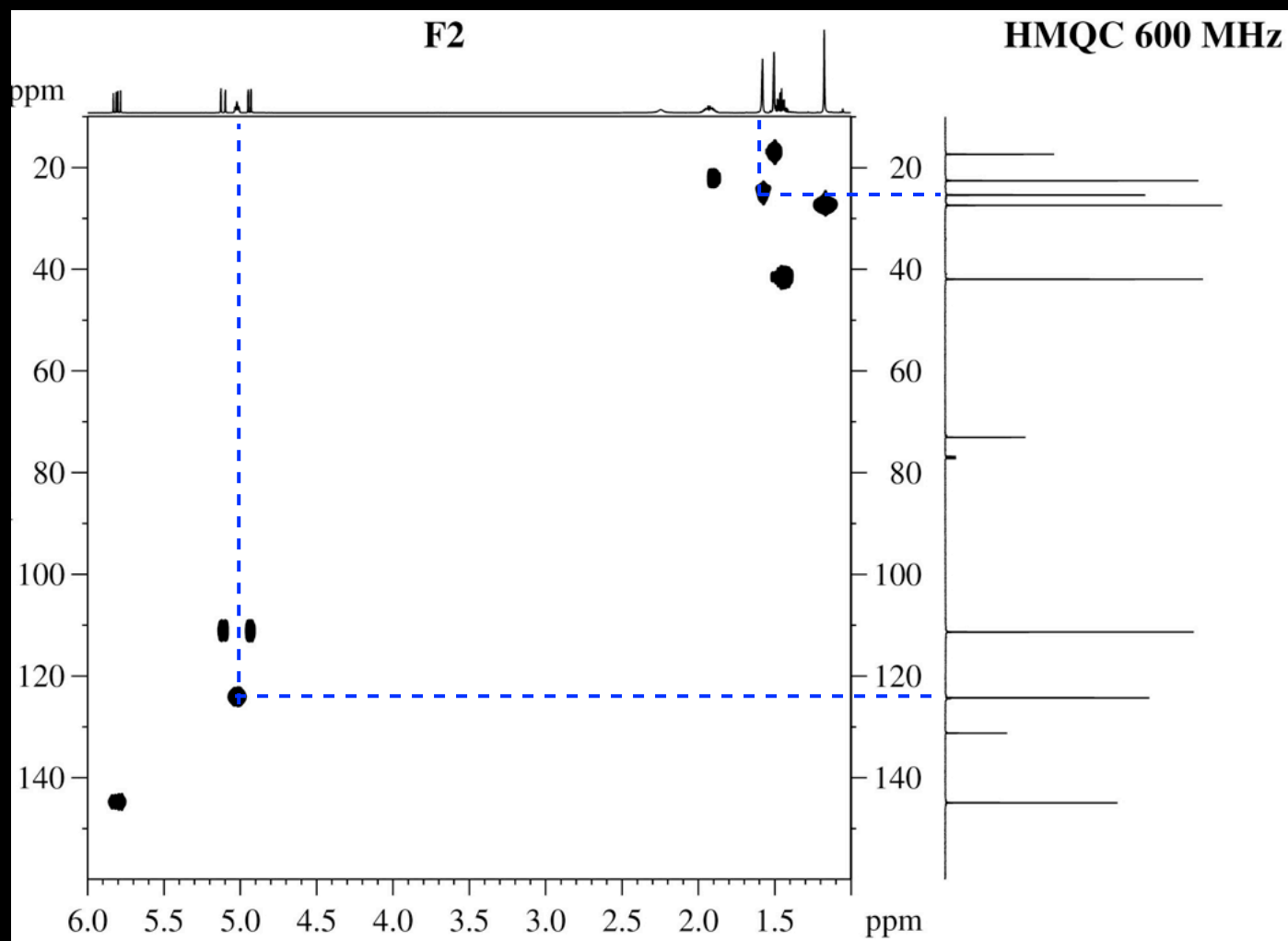


1 bond H-C coupling

2D NMR Spectroscopy

Who is Talking to Who?

HMQC

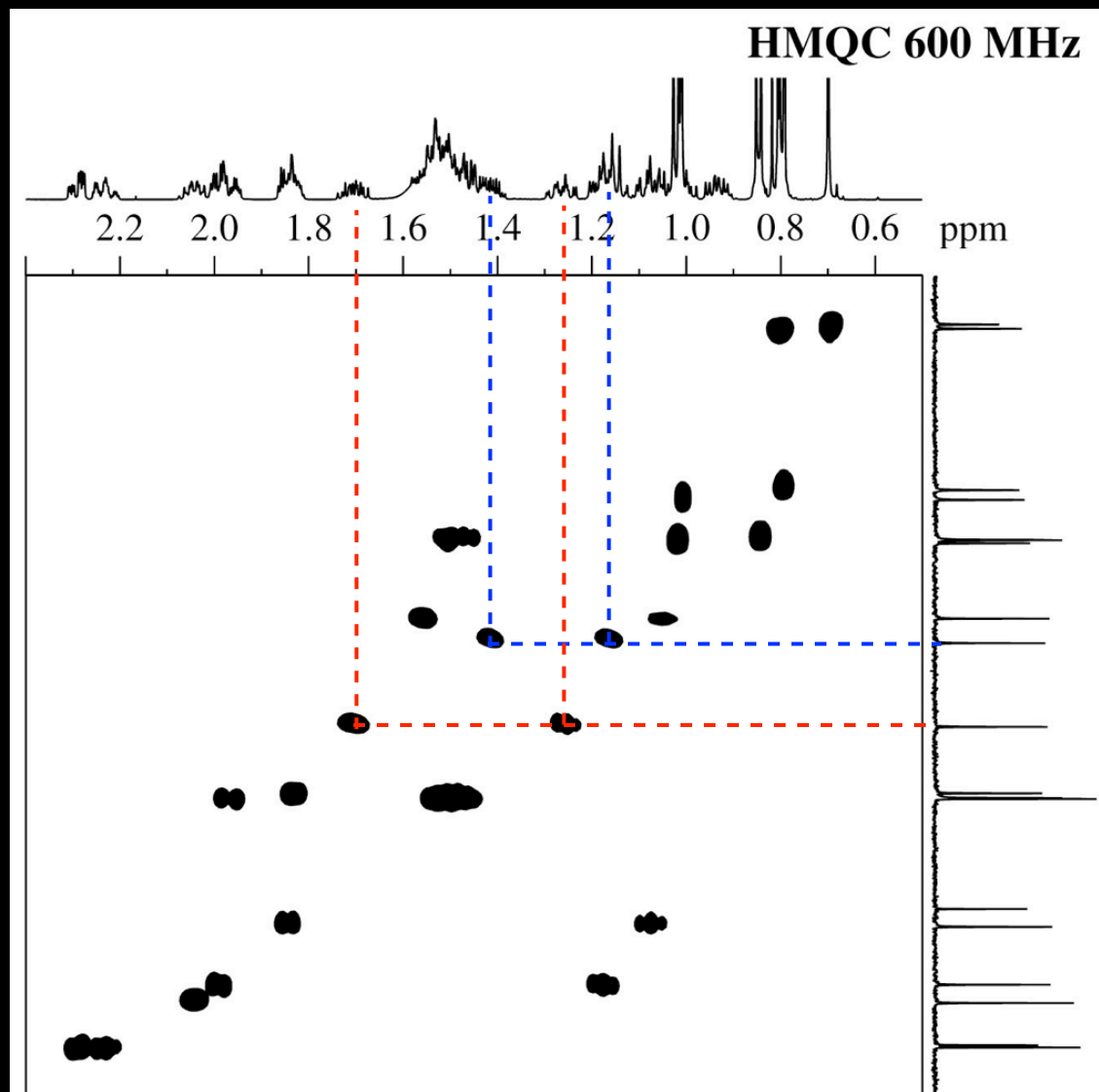


1 bond H-C coupling

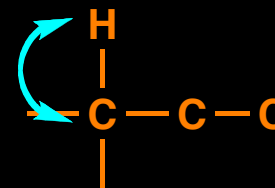
2D NMR Spectroscopy

Who is Talking to Who?

HMQC



Diastereotopic
Protons

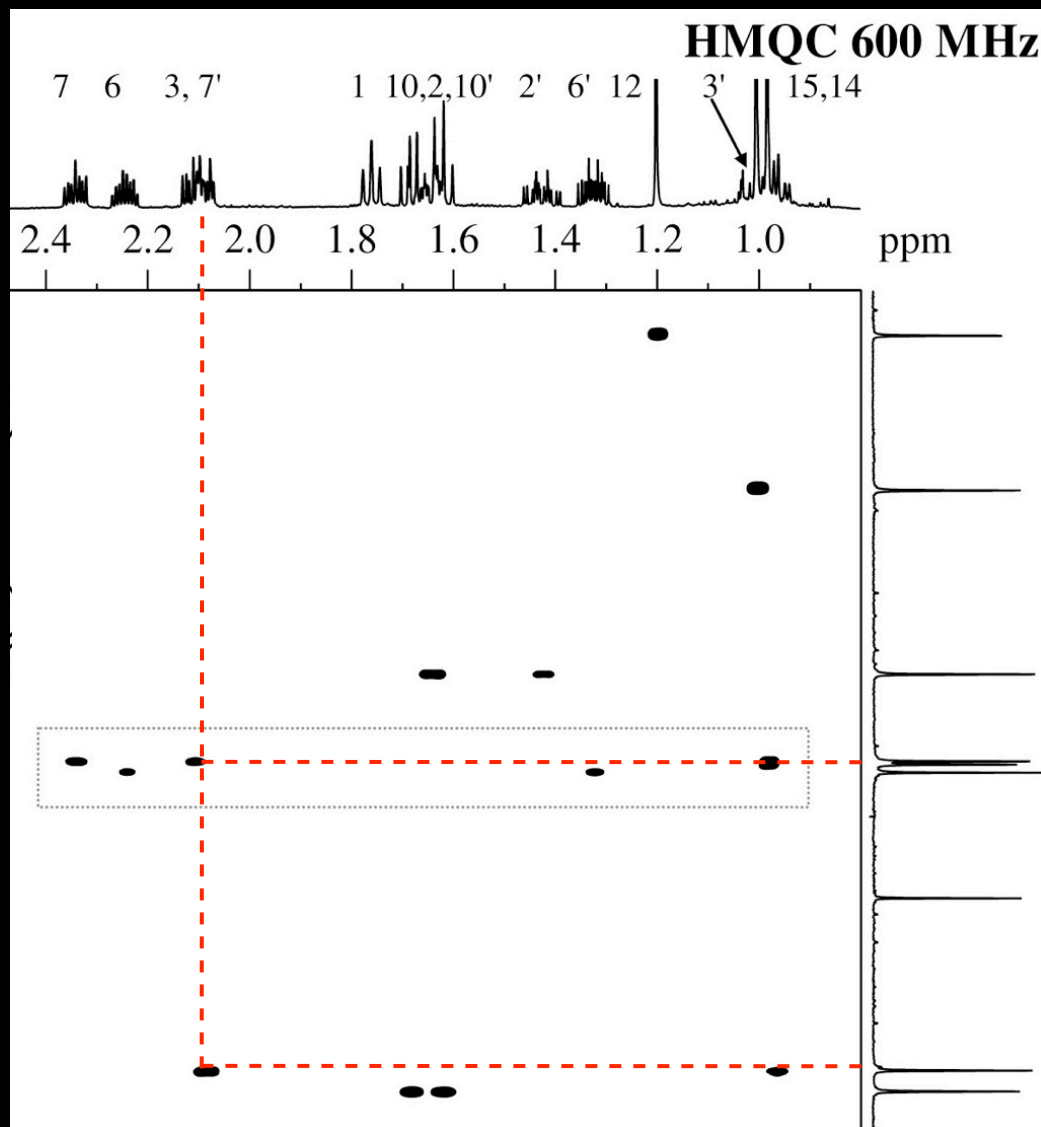


1 bond H-C coupling

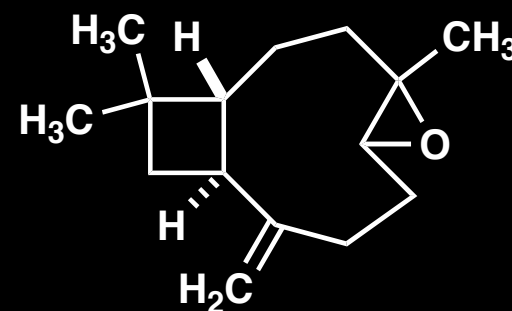
2D NMR Spectroscopy

Who is Talking to Who?

HMQC



Can “see into”
multiplets

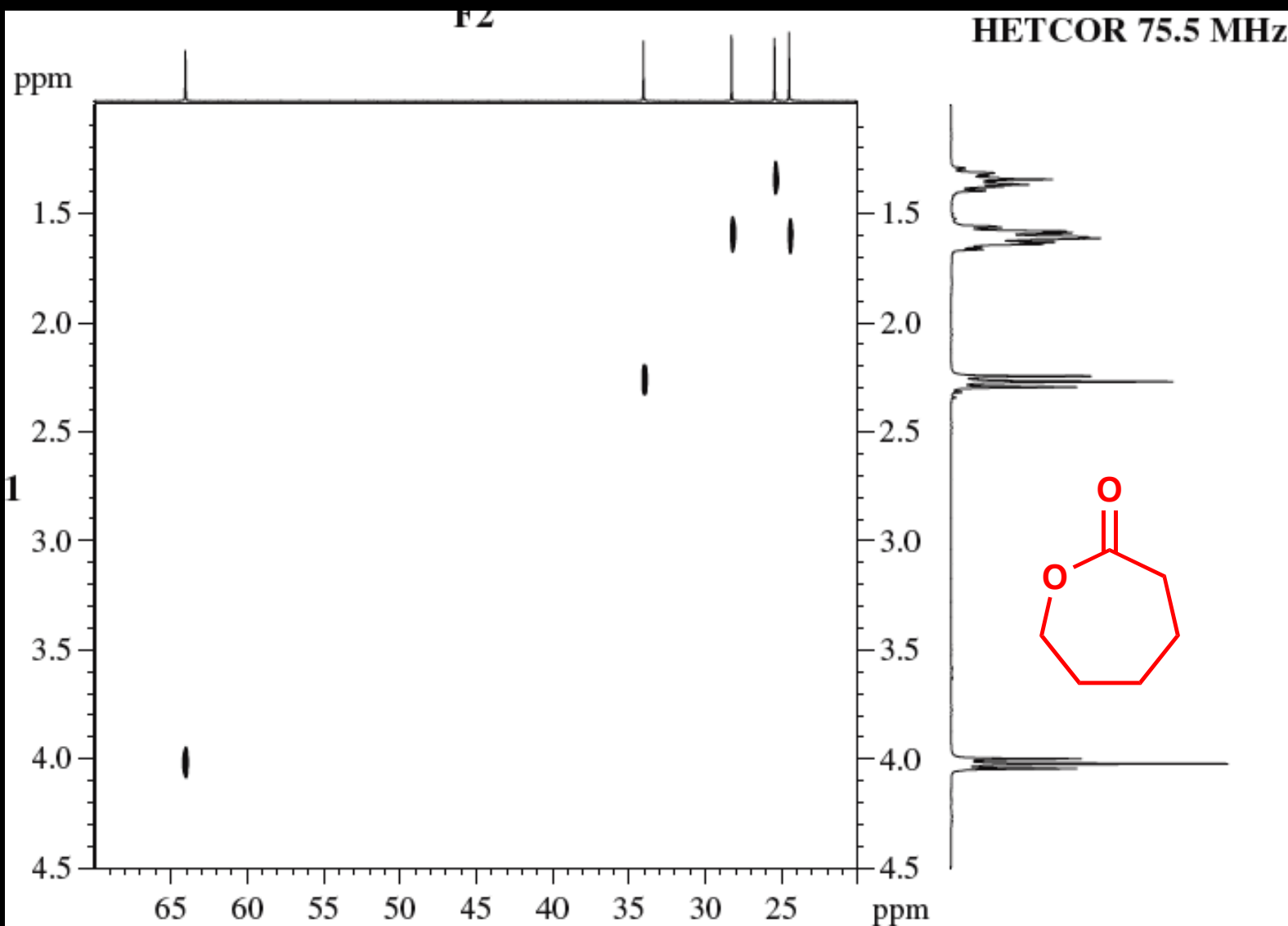


Caryophyllene Oxide

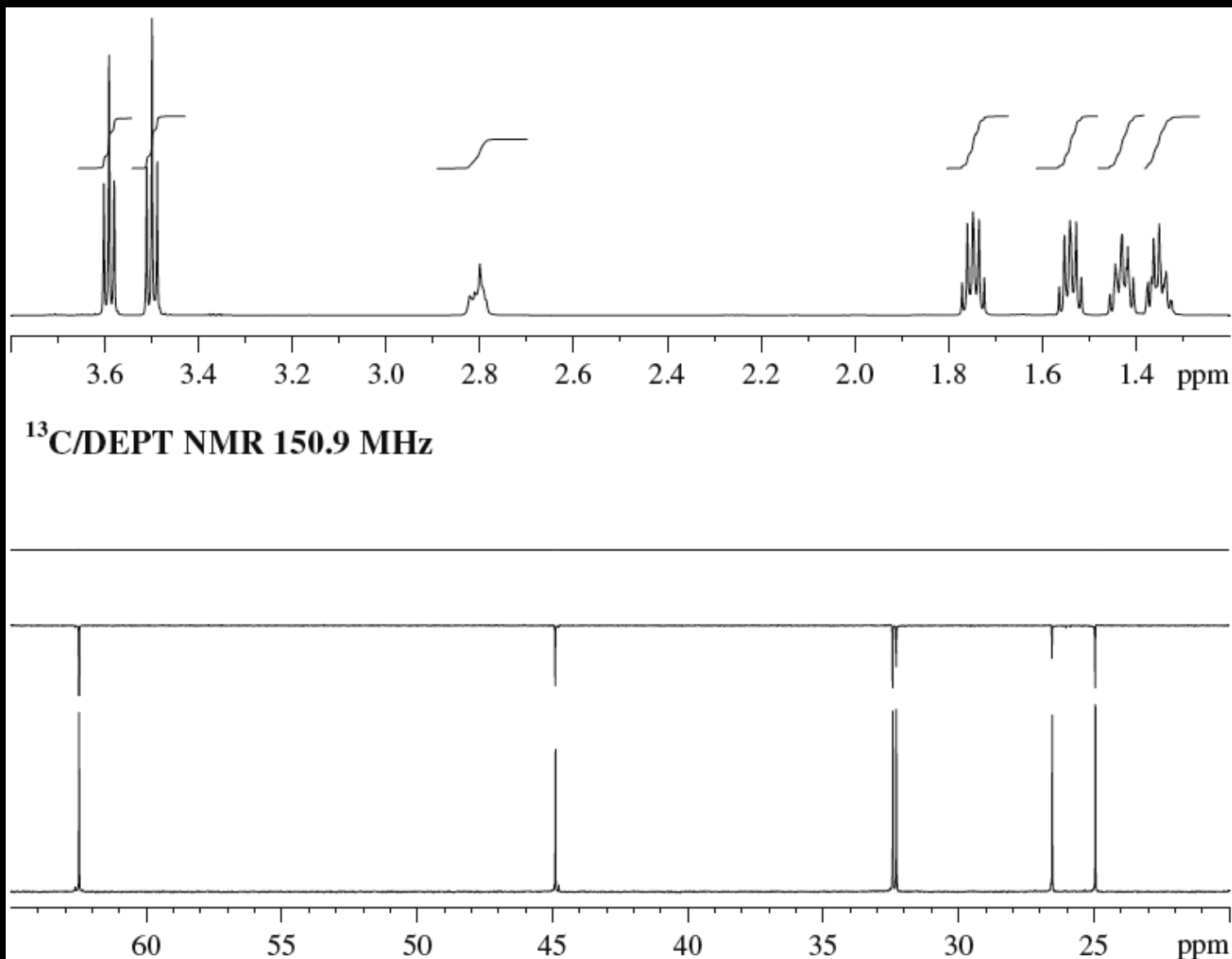
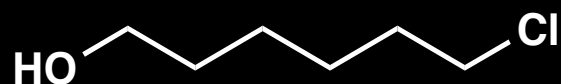
2D NMR Spectroscopy

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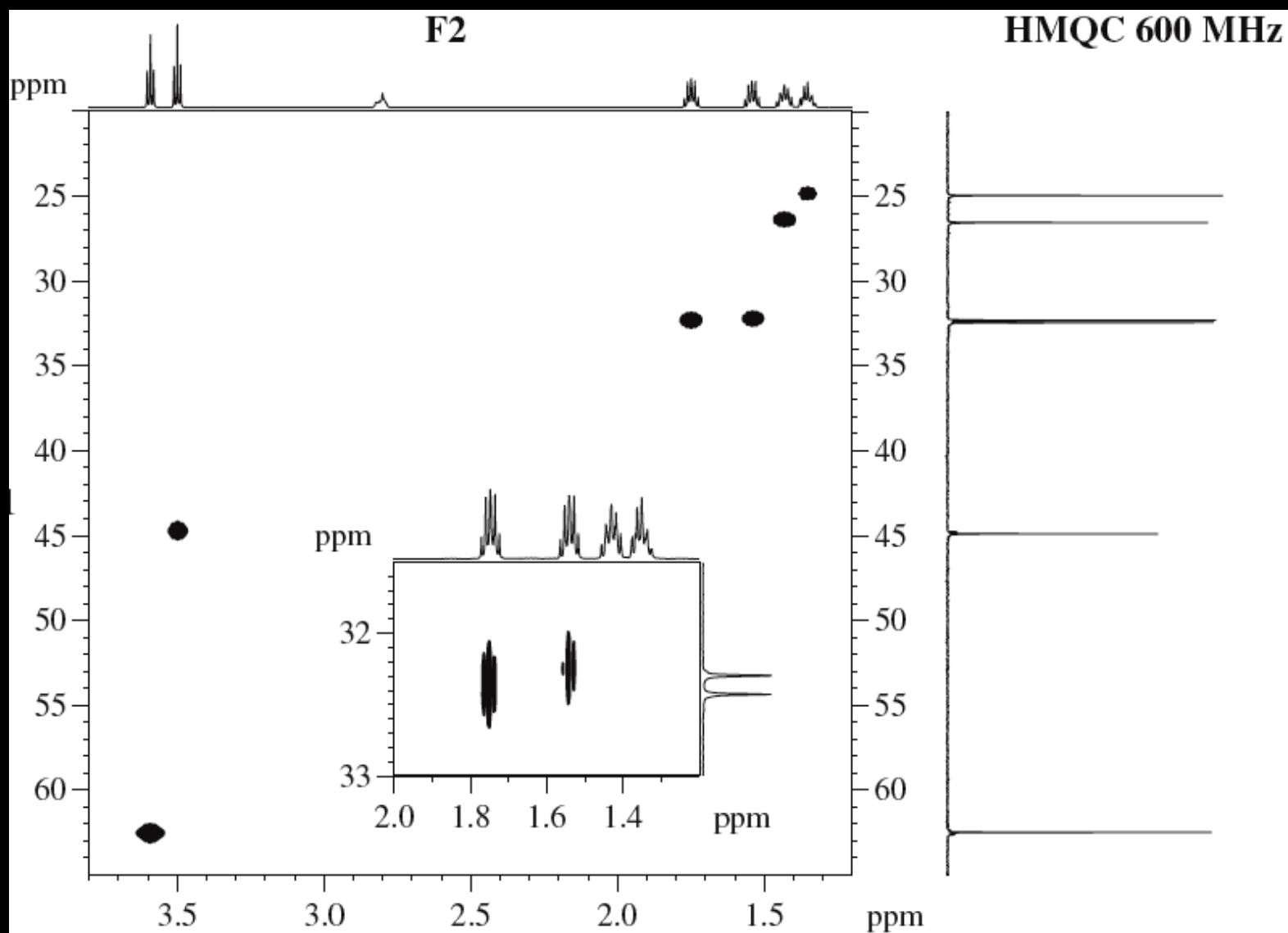
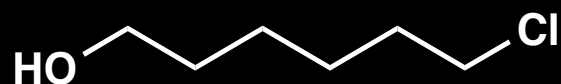
HMQC



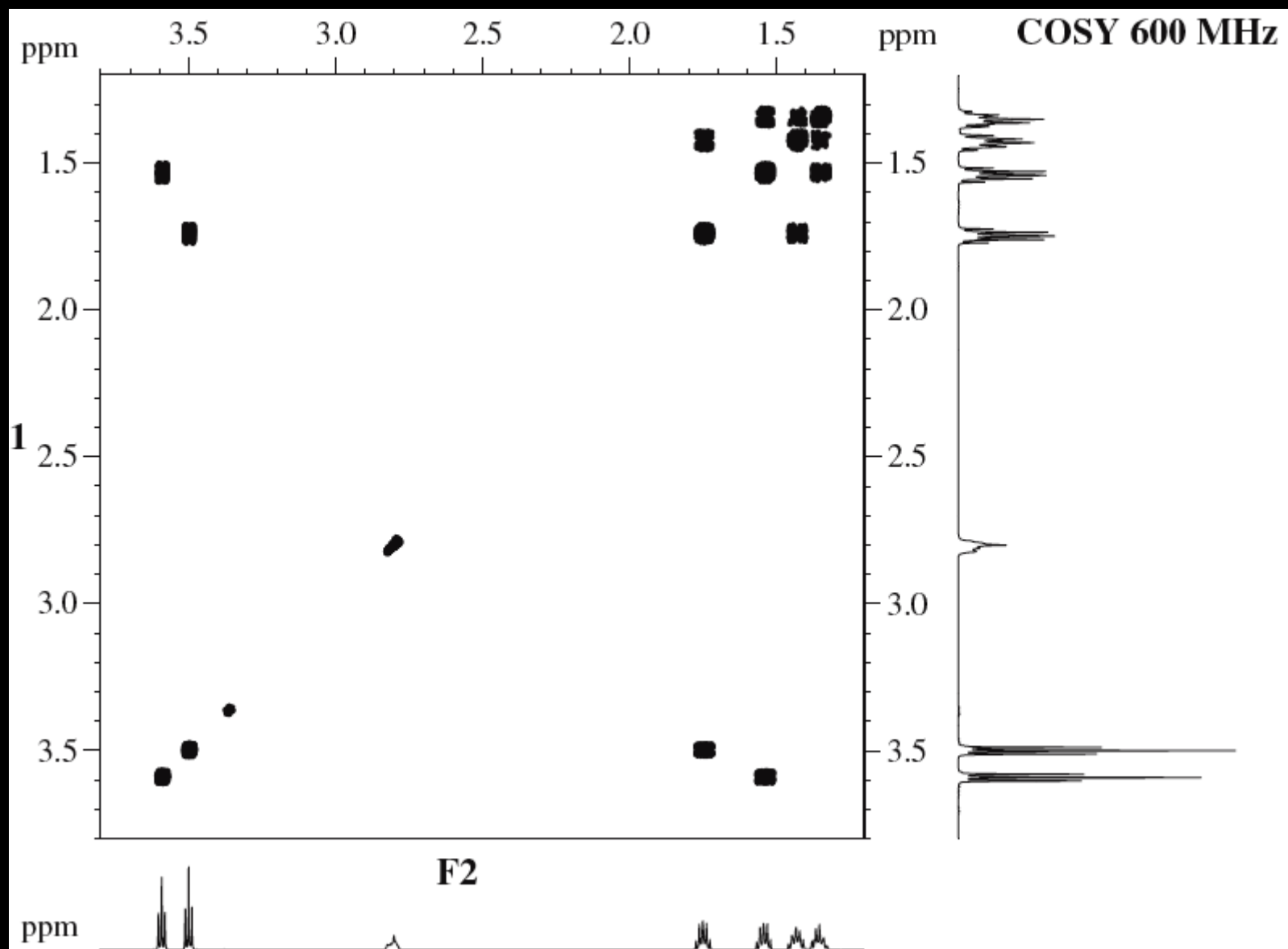
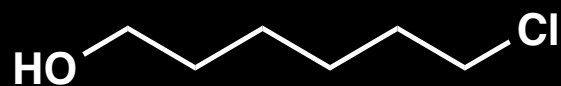
2D NMR Spectroscopy



2D NMR Spectroscopy



2D NMR Spectroscopy

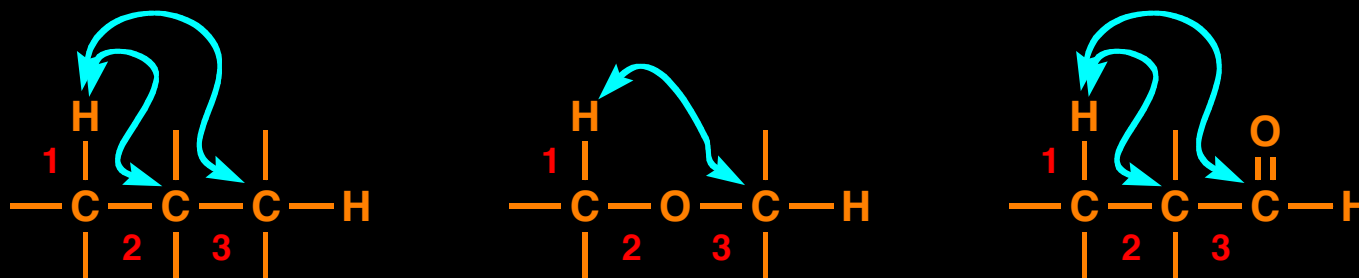


2D NMR Spectroscopy

Who is Talking to Who?

^1H - ^{13}C COSY (Long Range)

- COLOC (Correlated spectroscopy for Long range Couplings)
 - older experiment; ^{13}C -detected
- HMBC (Heteronuclear Multiple Bond Coherence)
 - newer experiment; ^1H -detected; completely replaced COLOC
- Both give same information, experimentally very different
- Peaks have two- or three-bond coupling
- “Sees through” heteroatoms and quaternary carbons
- Can be very complicated, but is very powerful

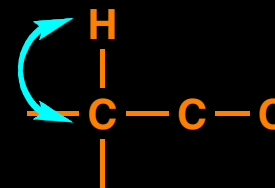
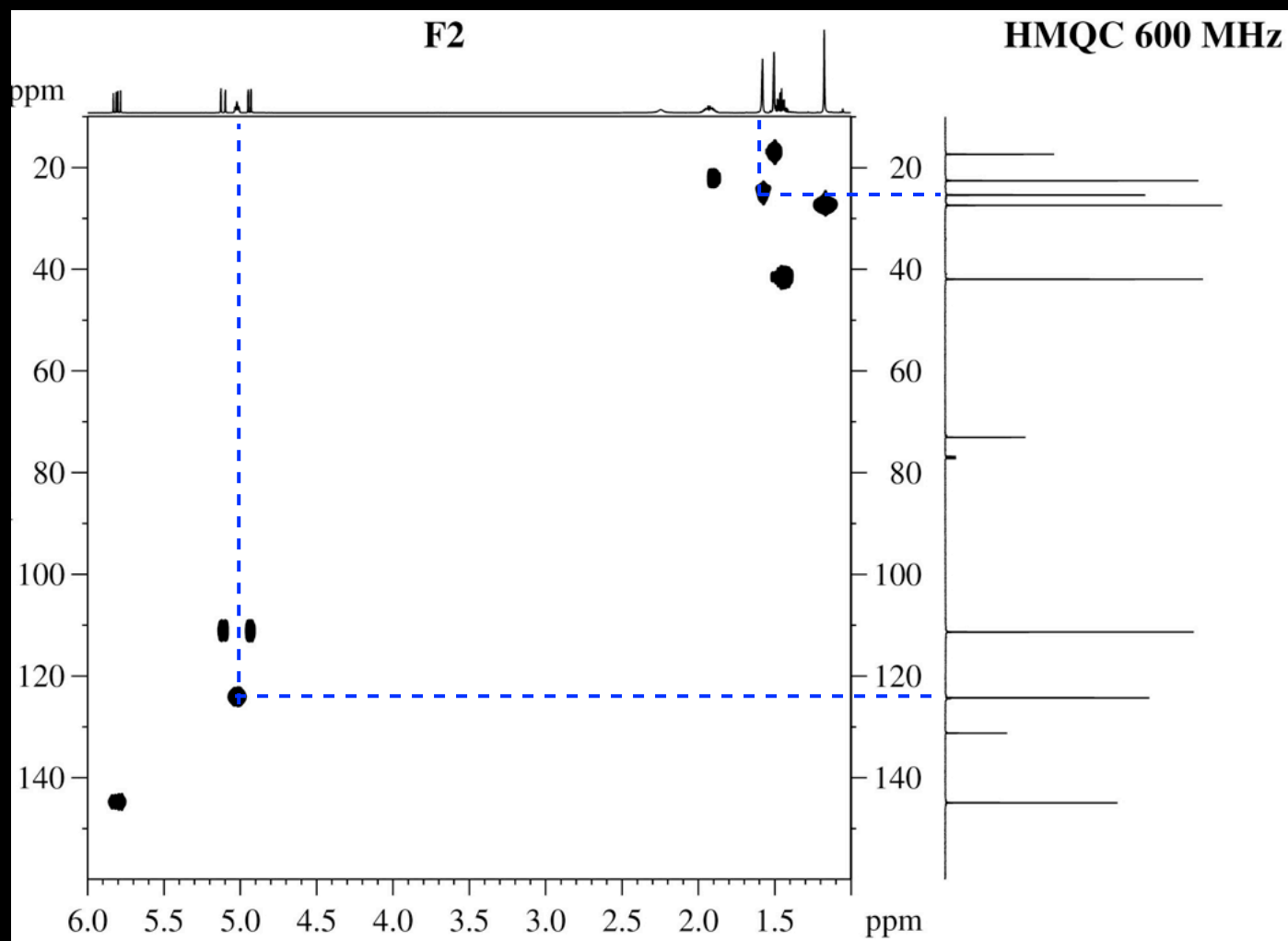


2 and 3 bond H-C couplings

2D NMR Spectroscopy

Who is Talking to Who?

HMQC

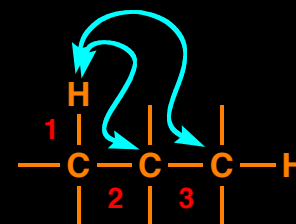
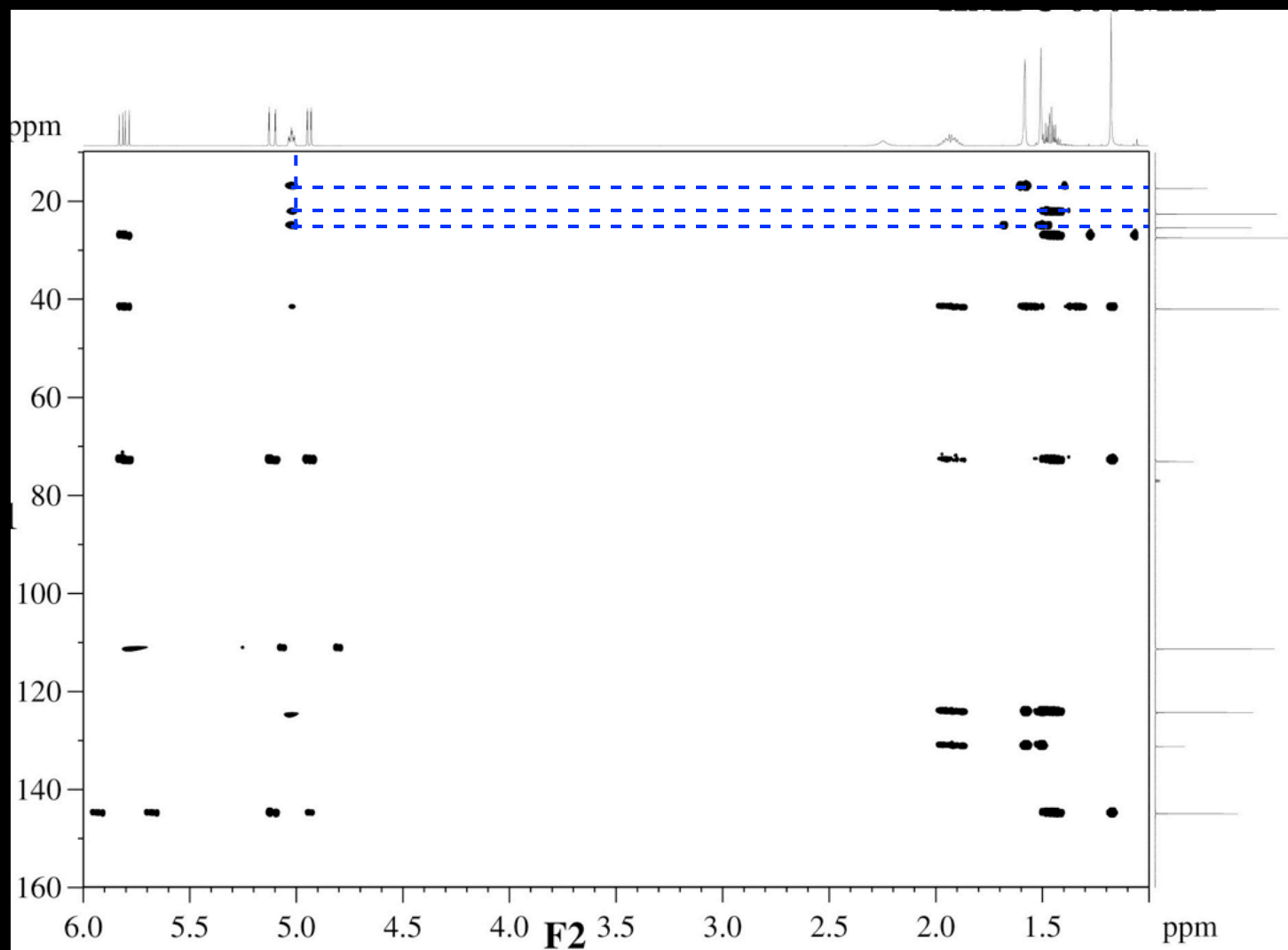


1 bond H-C coupling

2D NMR Spectroscopy

Who is Talking to Who?

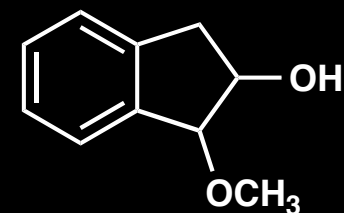
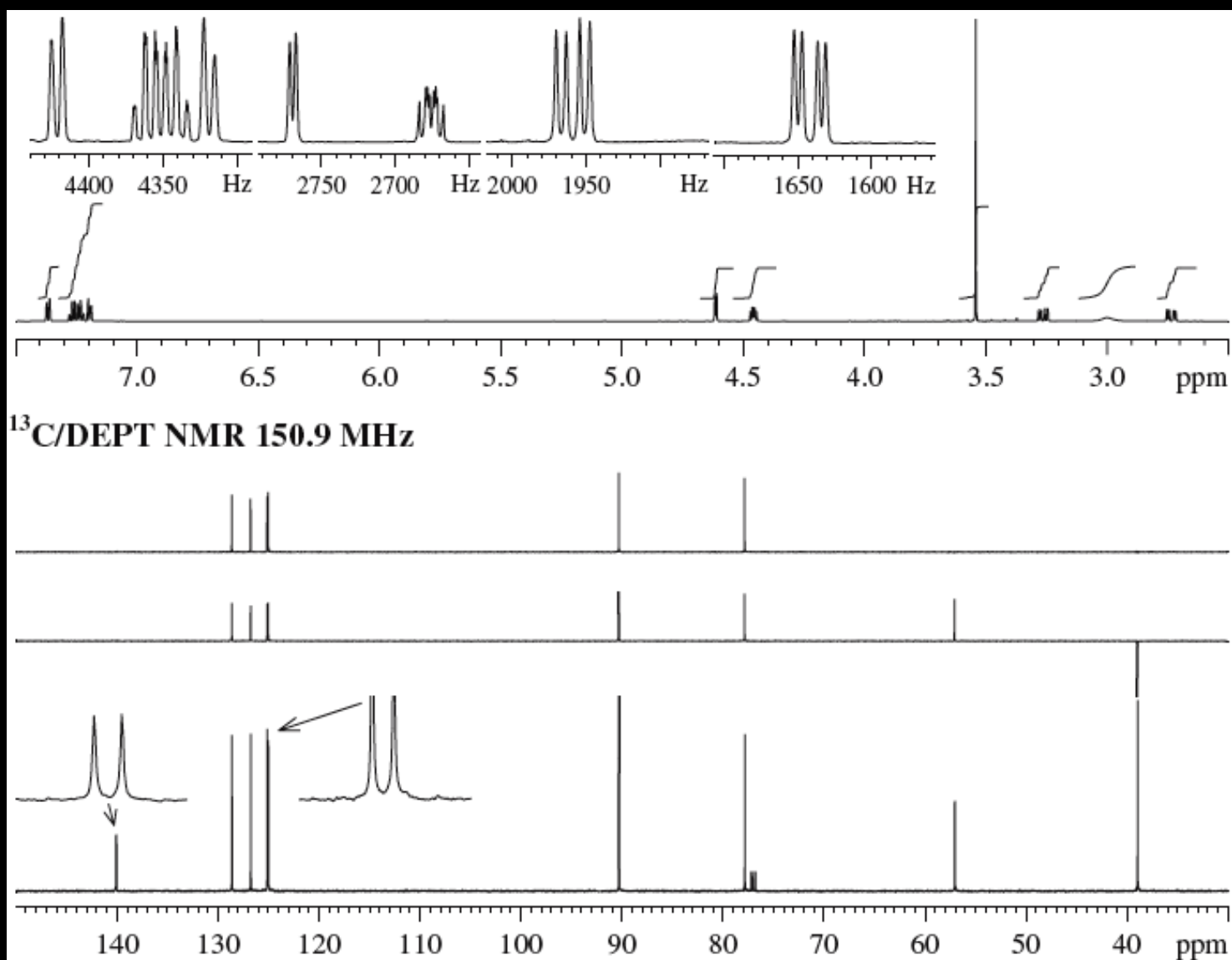
HMBC



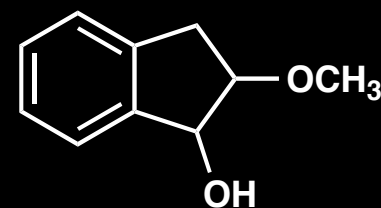
2 and 3 bond H-C couplings

2D NMR Spectroscopy

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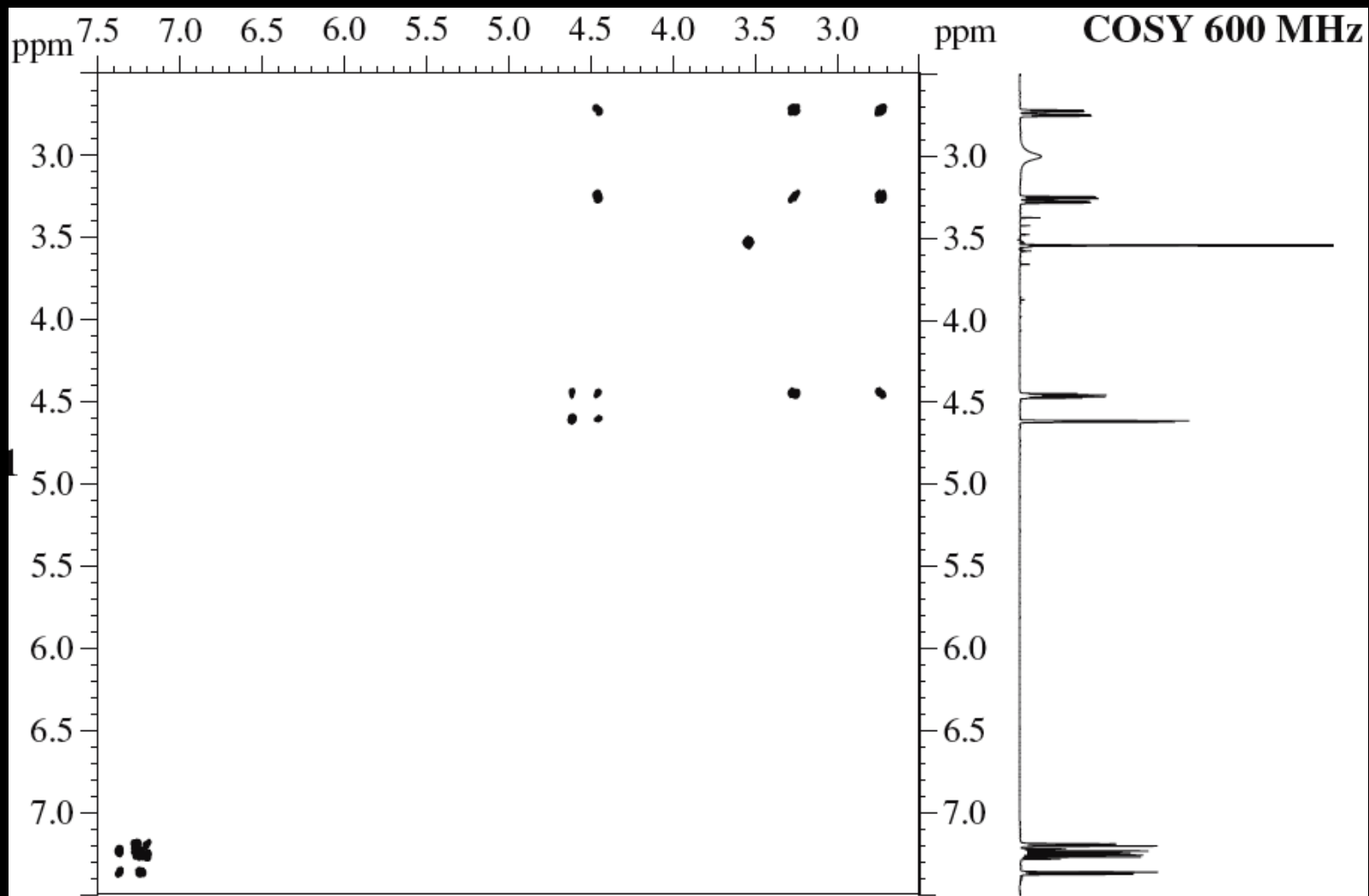
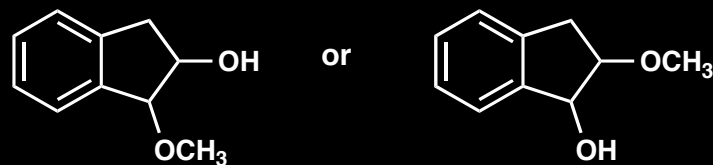


or



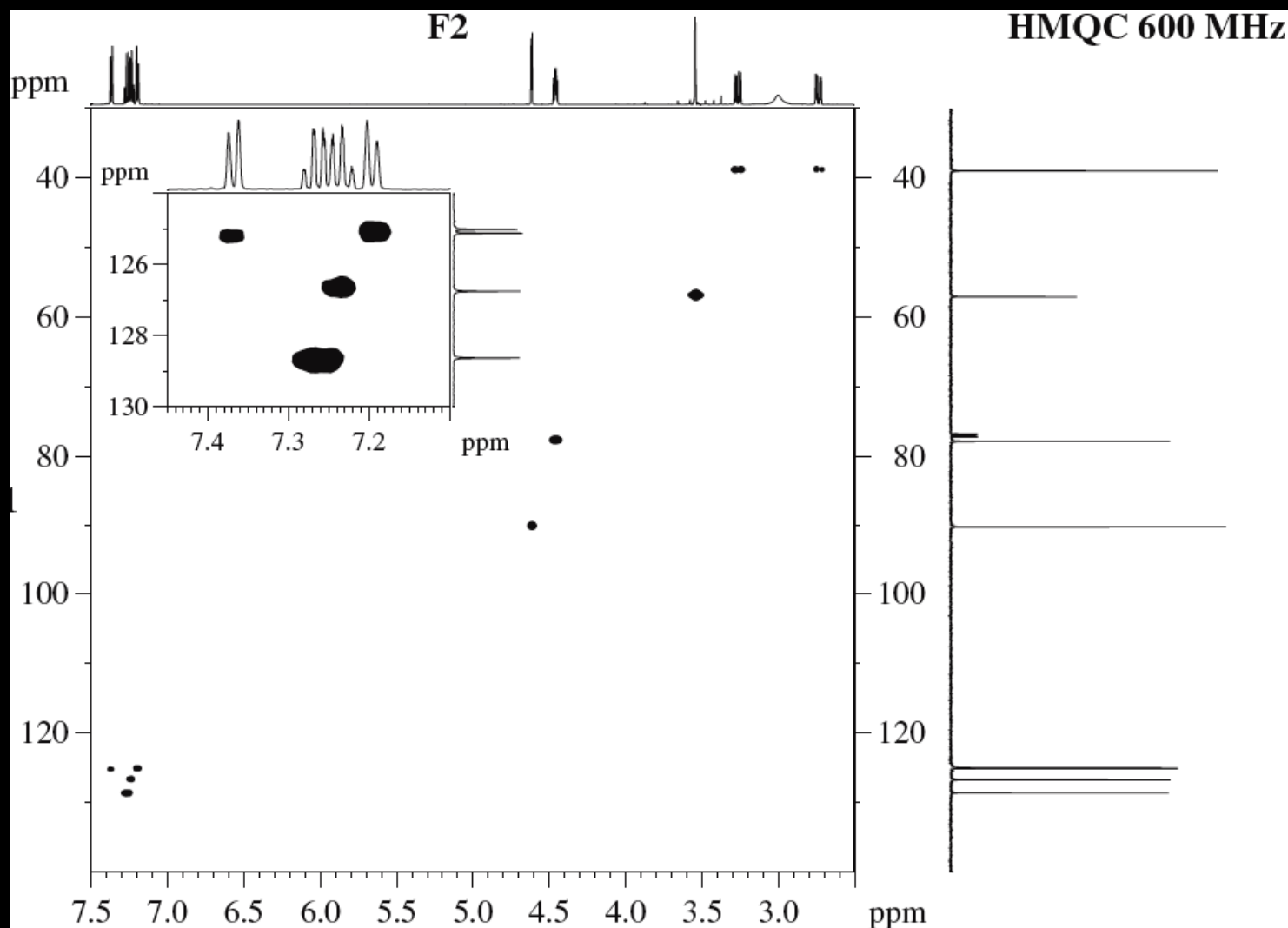
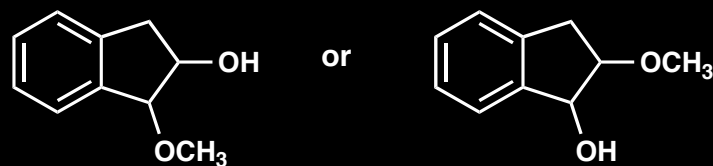
2D NMR Spectroscopy

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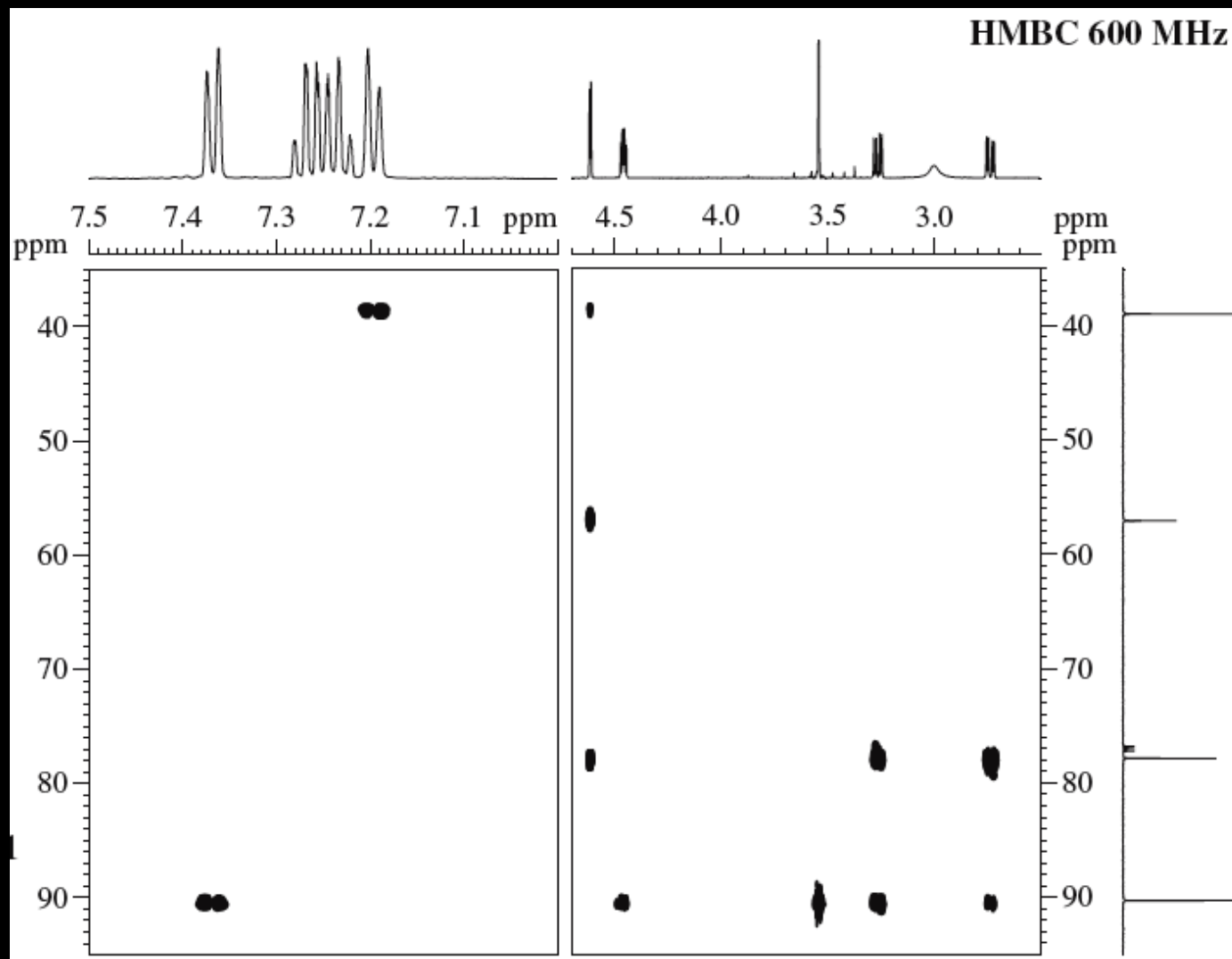
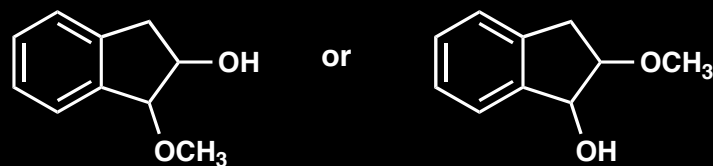
2D NMR Spectroscopy

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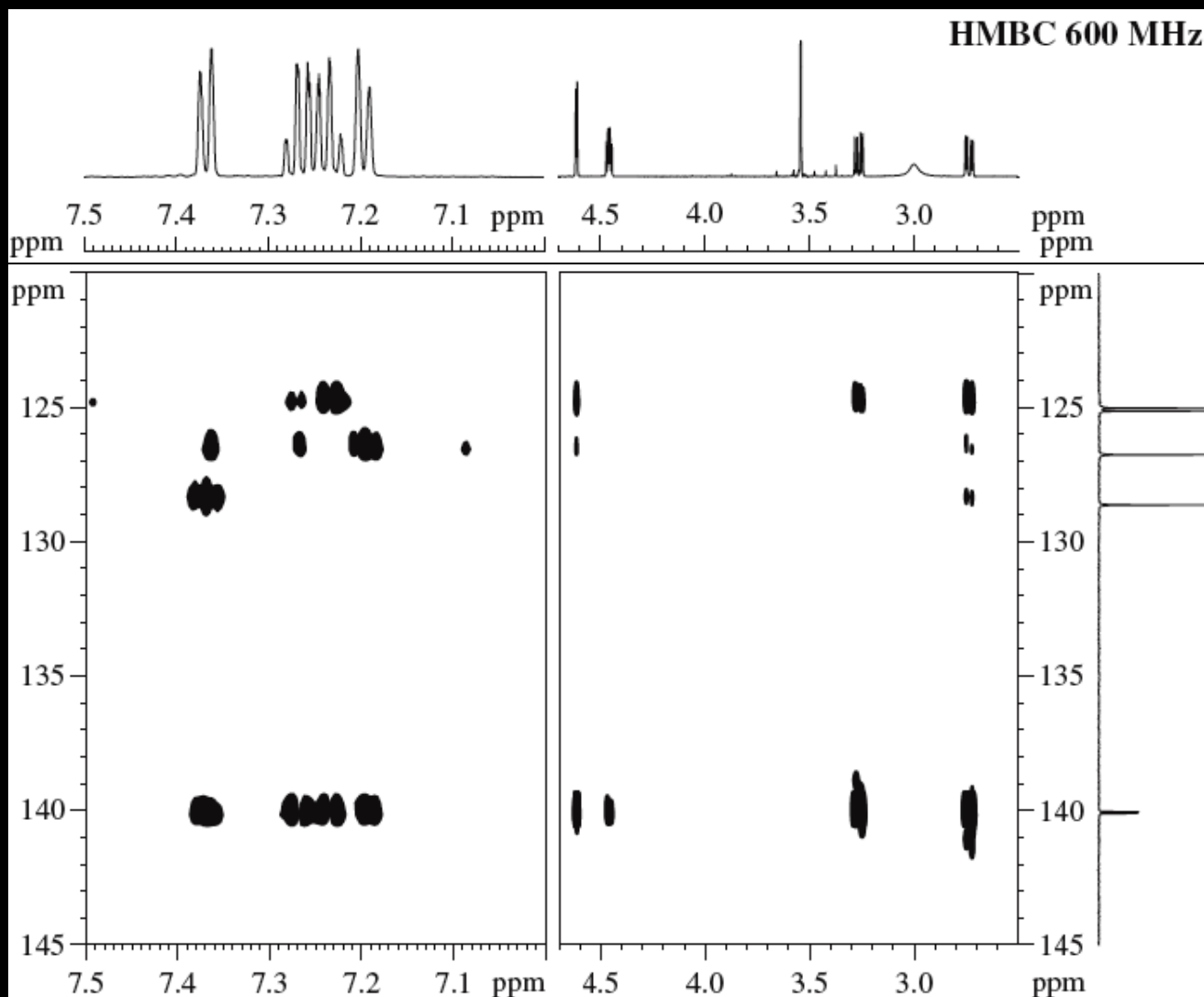
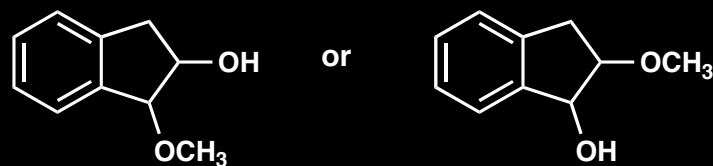
2D NMR Spectroscopy

Who is Talking to Who?



2D NMR Spectroscopy

Who is Talking to Who?



2D NMR Spectroscopy

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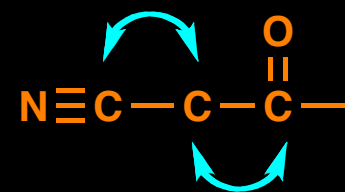
^{13}C – ^{13}C COSY

- INADEQUATE (Incredible Natural Abundance Double Quantum Transfer Experiment)
- tells what carbons are attached to each other
- if you know what type of carbon it is (C, C=O, CH, CH₂, CH₃, etc.) from DEPT, you can almost write down the entire gross structure by running two NMR experiments

– **BUT** it is ^{13}C – ^{13}C coupling

- probability of one ^{13}C is 0.01
- two next to each other $0.01 \times 0.01 = 0.0001$
(~1 molecule in 10,000)

- Need lots of sample and instrument time to overcome
- In our facility: 80% v/v, overnight, 500 MHz = nothing

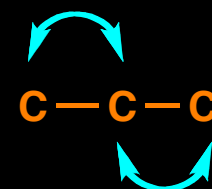
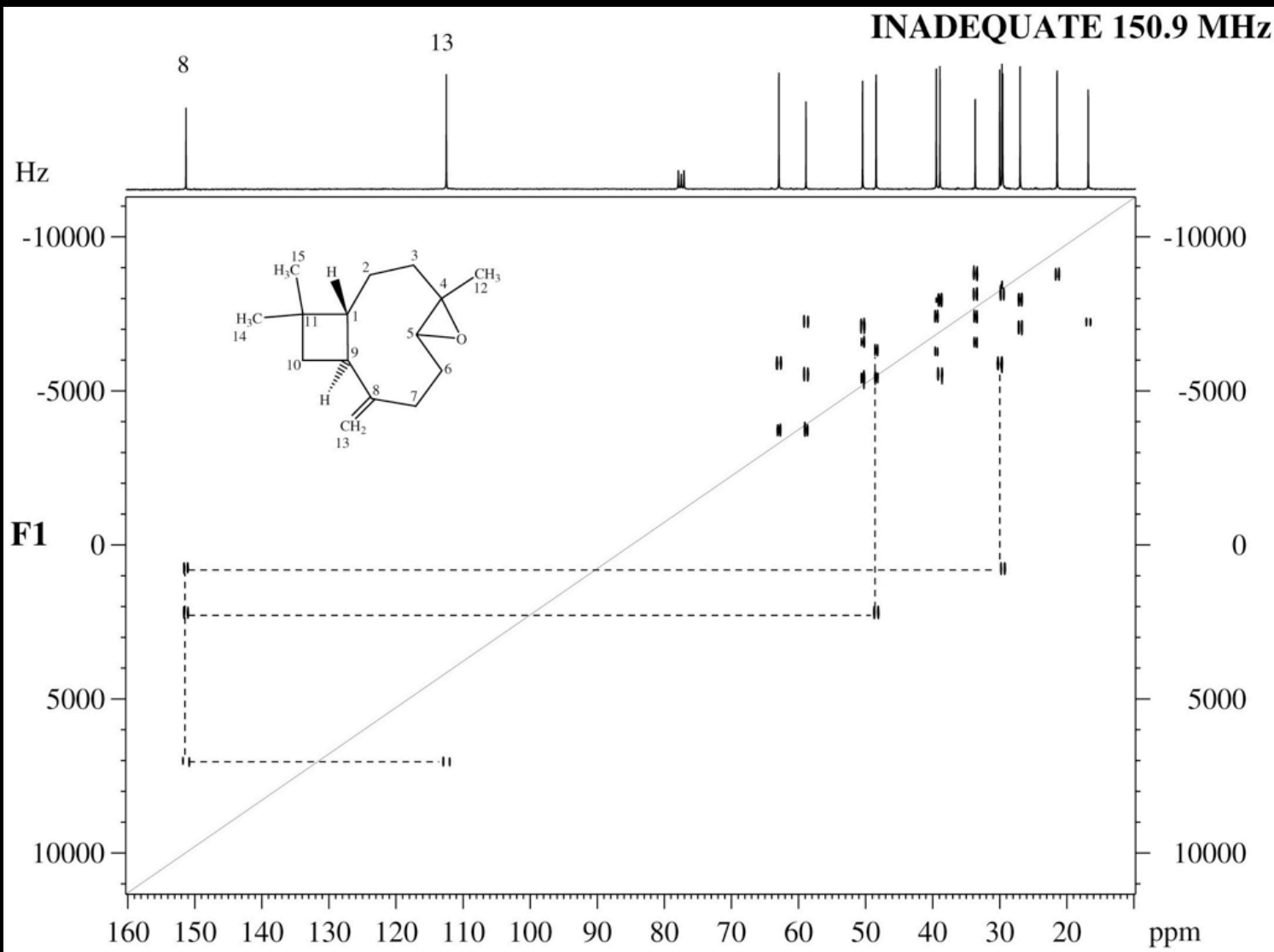


1 bond C–C coupling

2D NMR Spectroscopy

Who is Talking to Who?

INADEQUATE



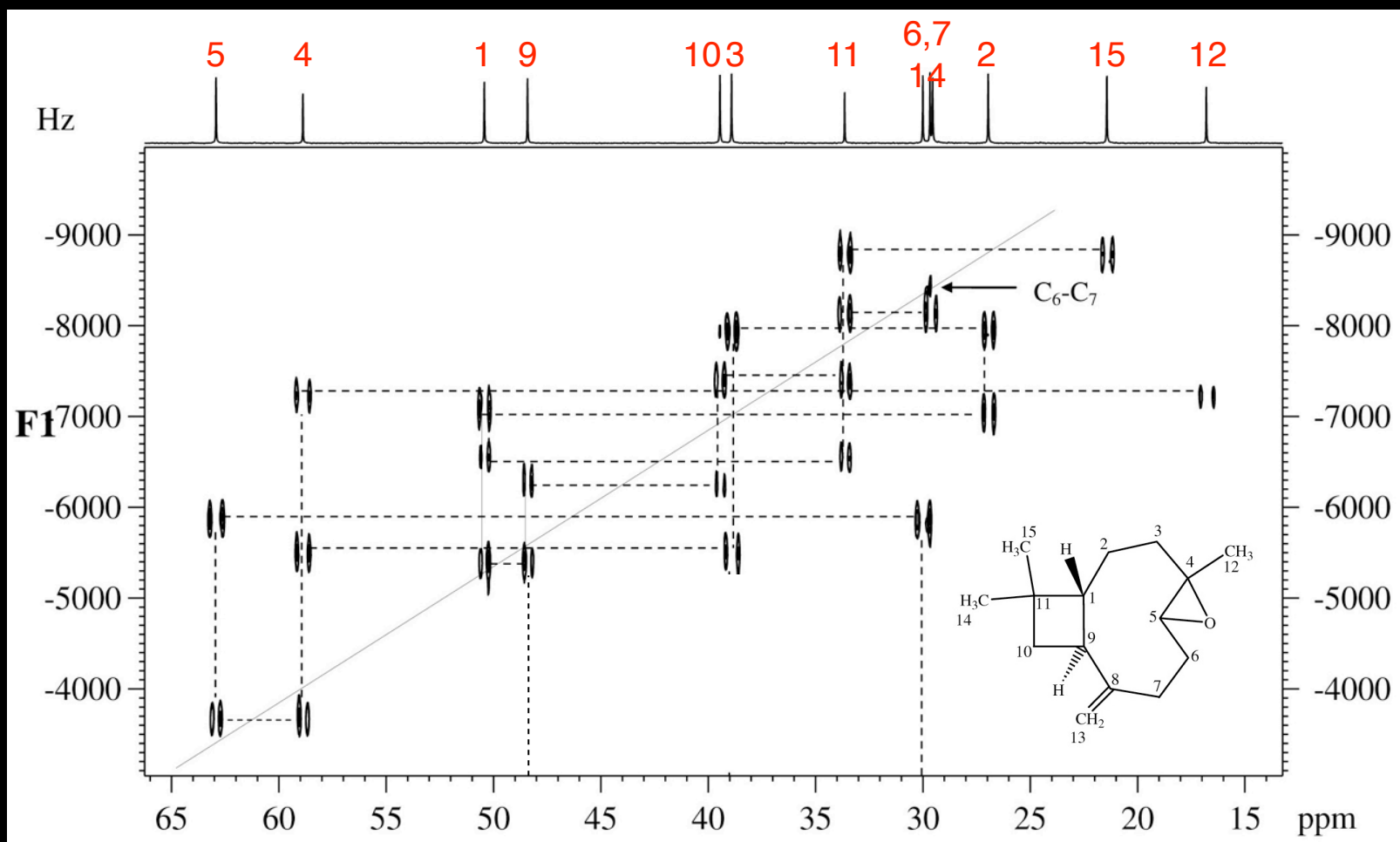
1 bond C-C coupling

2D NMR Spectroscopy

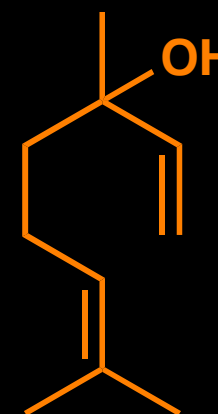
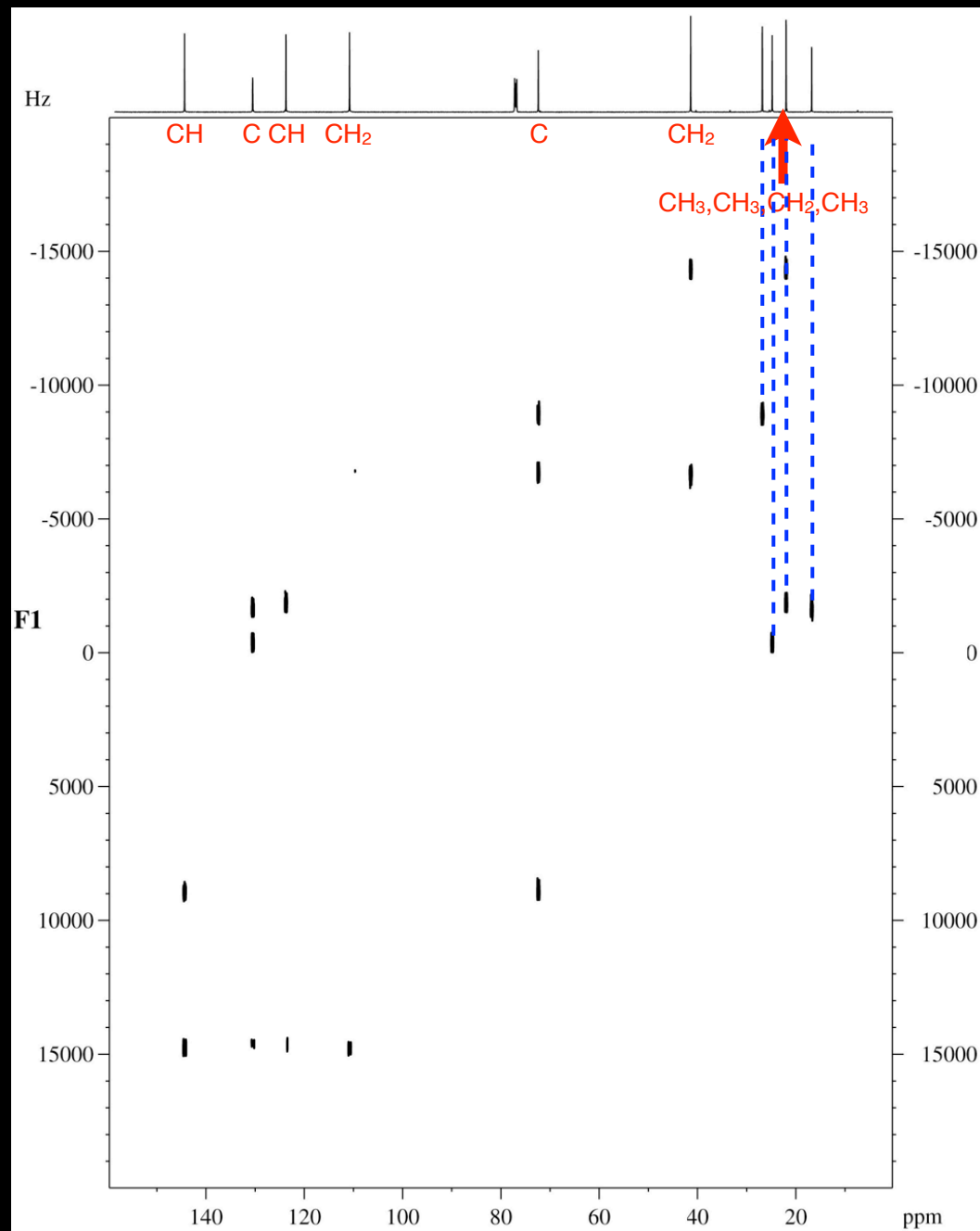
Who is Talking to Who?

INADEQUATE

- Cross peaks show up as doublets = J_{CC}
- Diagonal is midway between the two doublets

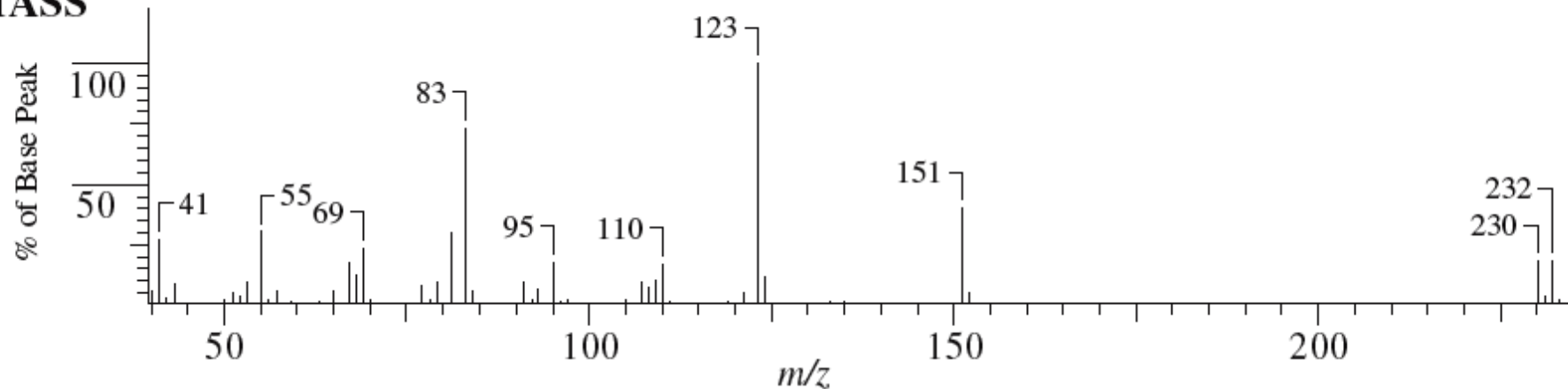


2D NMR Spectroscopy

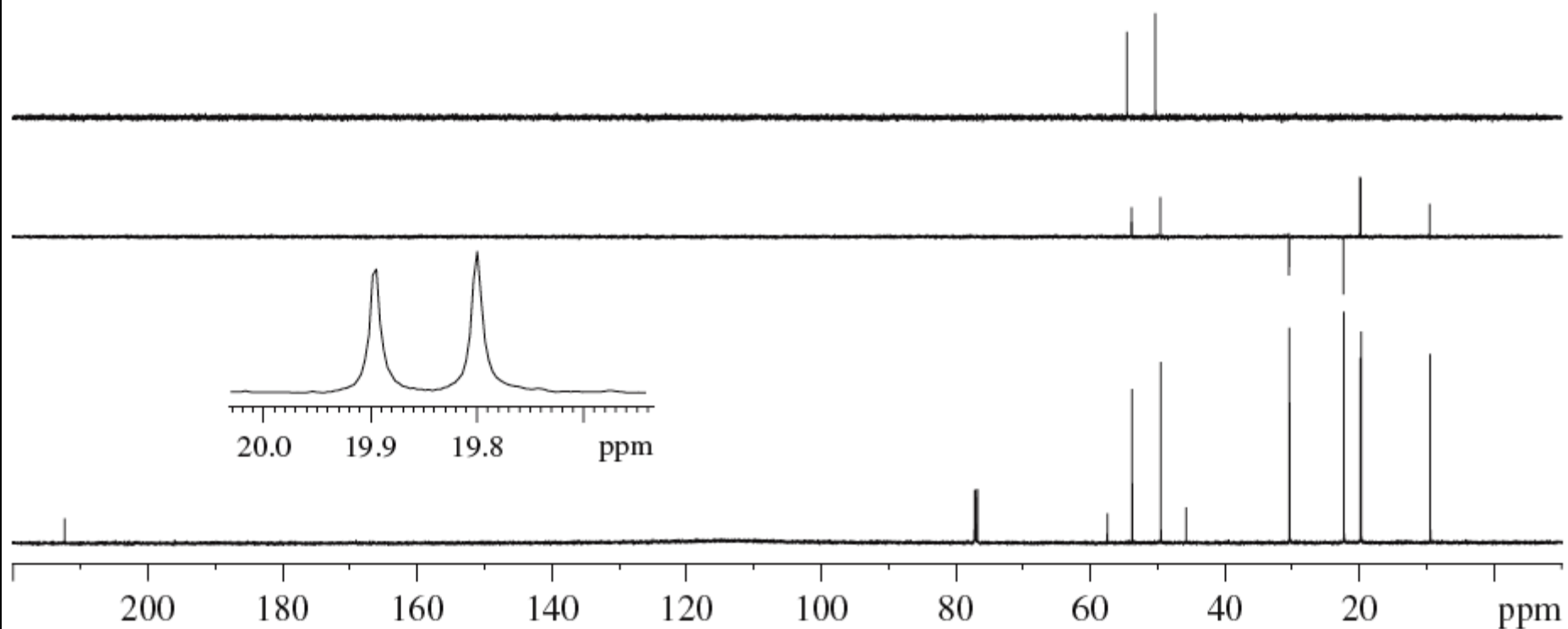


2D NMR Spectroscopy

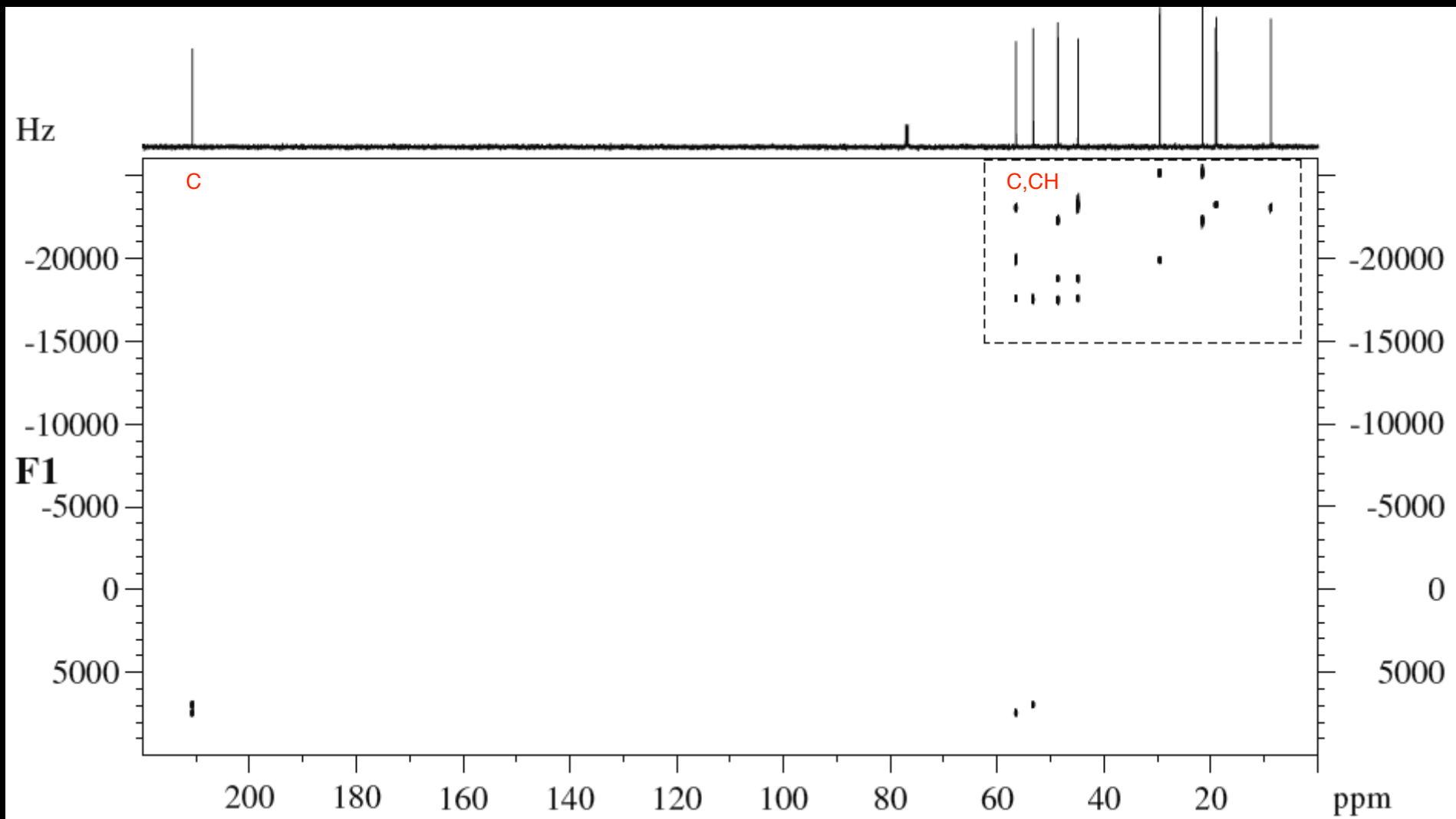
MASS



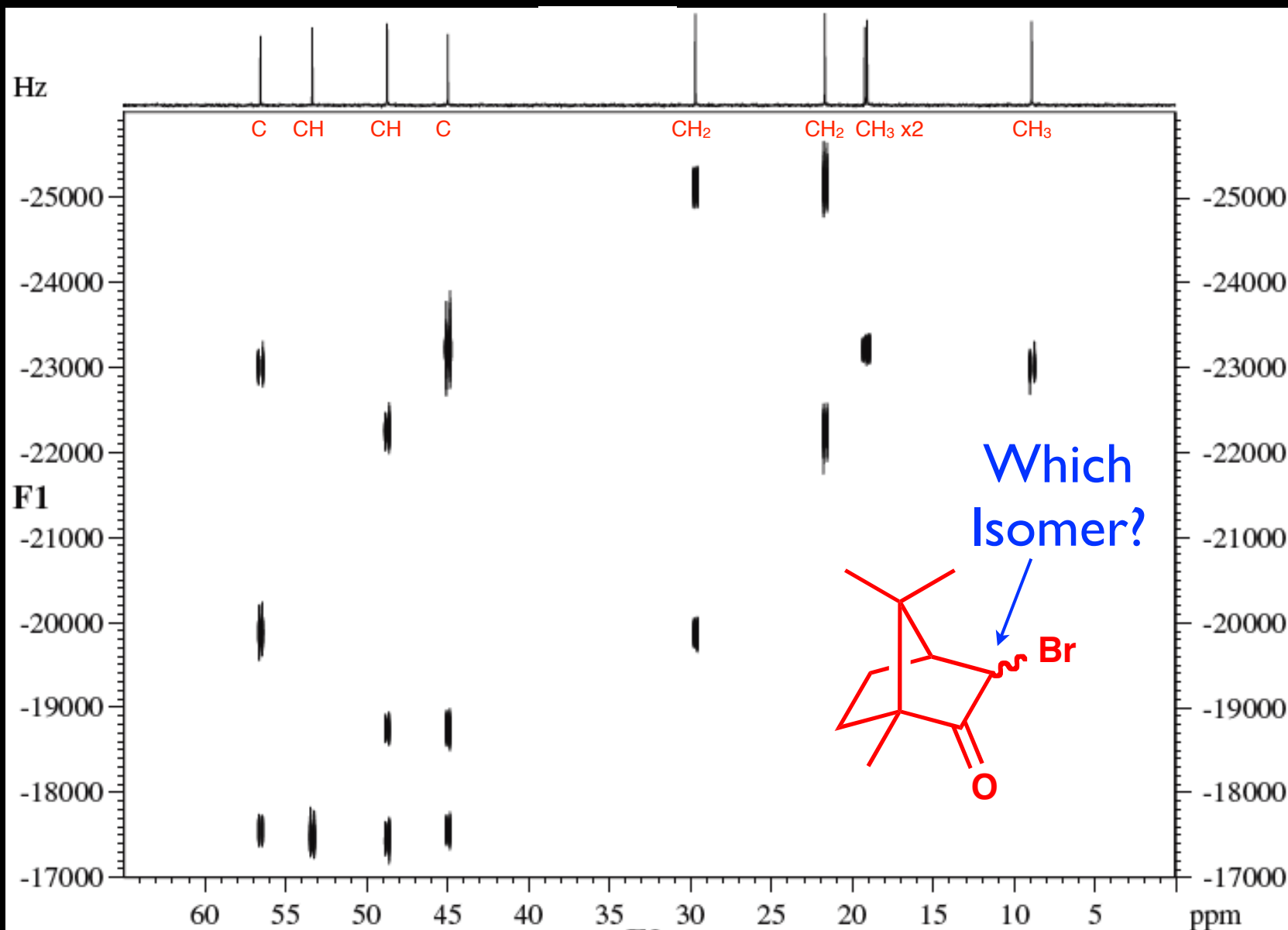
$^{13}\text{C}/\text{DEPT}$ NMR 150.9 MHz



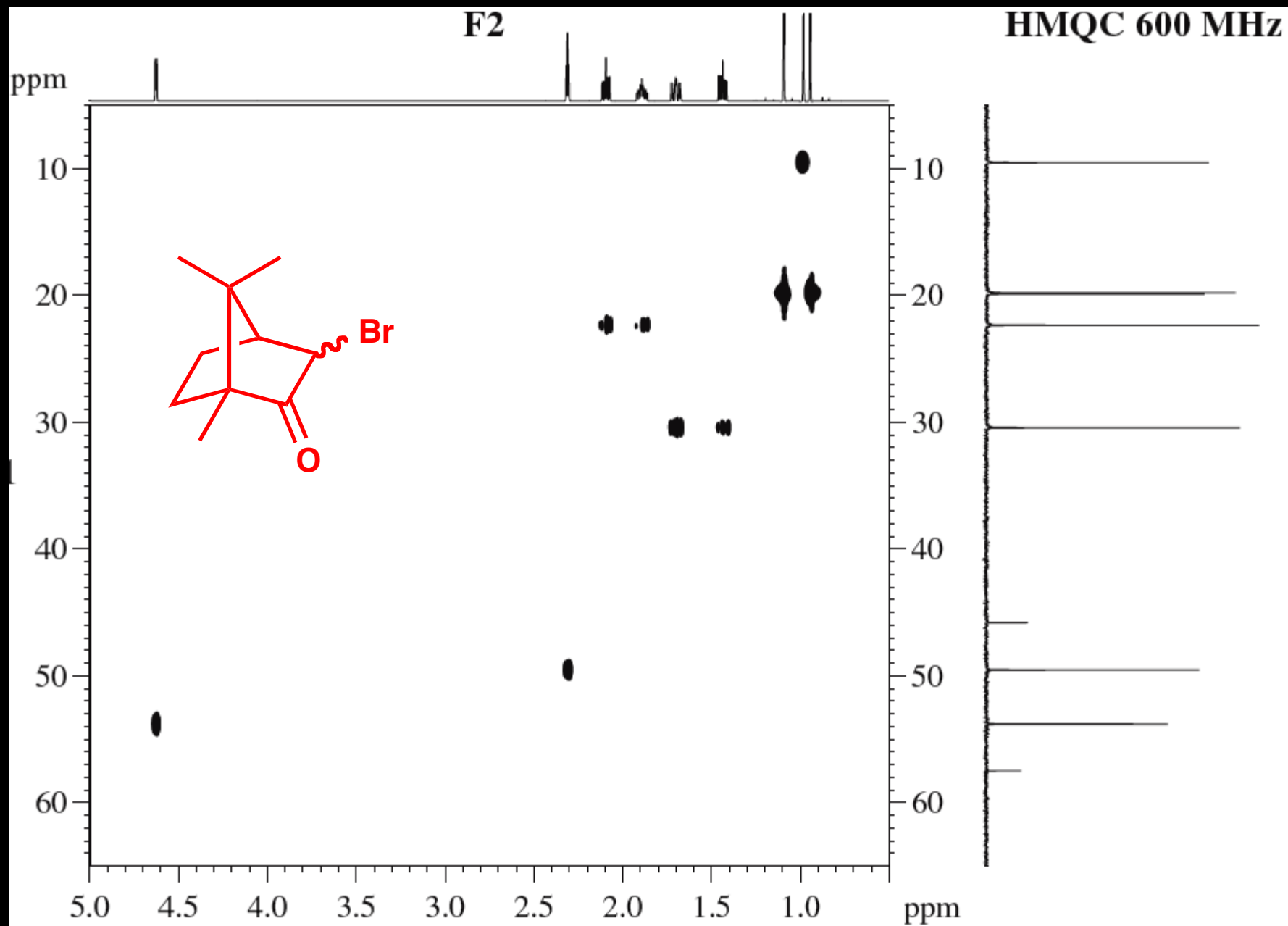
2D NMR Spectroscopy



2D NMR Spectroscopy



2D NMR Spectroscopy



2D NMR Spectroscopy

