Multidimensional NMR Experiments

Chem 8361/4361:
Interpretation of Organic Spectra

2D NMR Spectroscopy

General Information

- More complicated experiments to set up than ^{1}H 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

http://www.chem.ox.ac.uk/spectroscopy/nmr/acropage.htm

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 ^{1}H-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 protons, can get a rough idea of molecular weight

2D NMR Spectroscopy

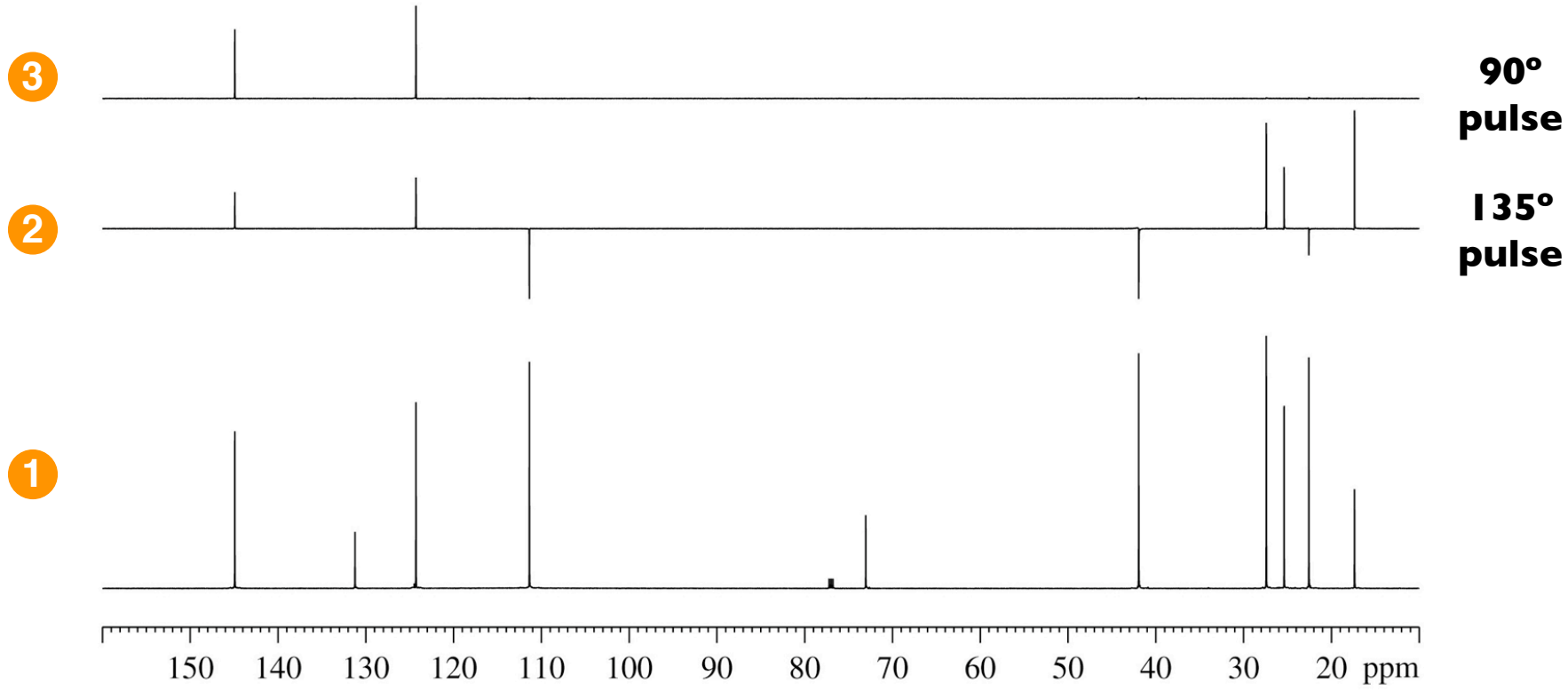
Number of Protons on Carbon

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

1 = Carbon spectrum

2 = ↓ CH_2
↑ CH, CH_3

3 = ↑ CH

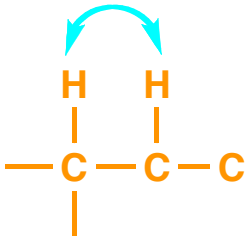


2D NMR Spectroscopy

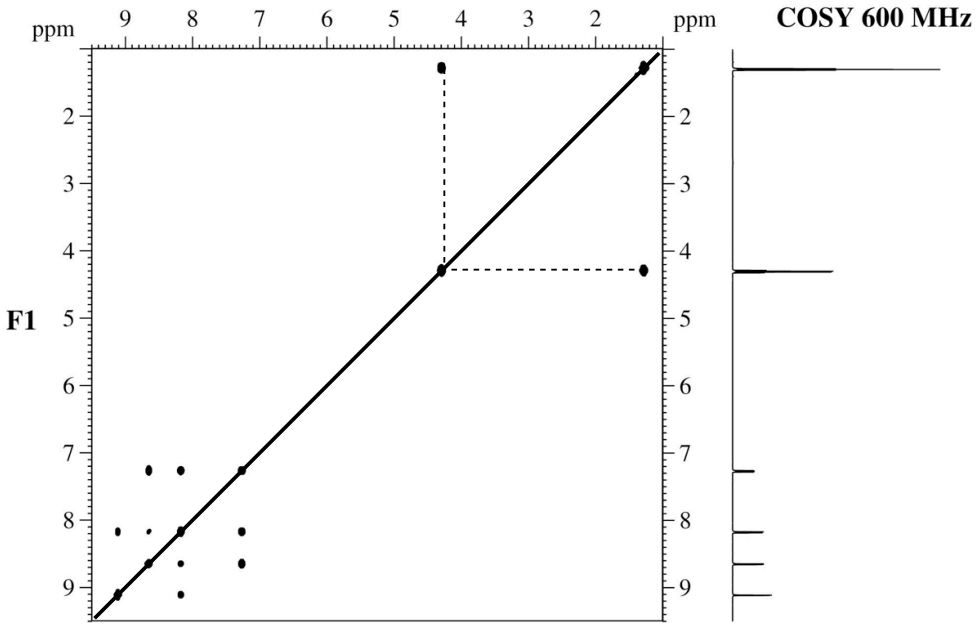
Who is Talking to Who?

^{1}H–^{1}H COSY (Correlation Spectroscopy)

- Tells you how which protons are coupled to one another
- Very useful when peaks are overlapping in ^{1}H 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



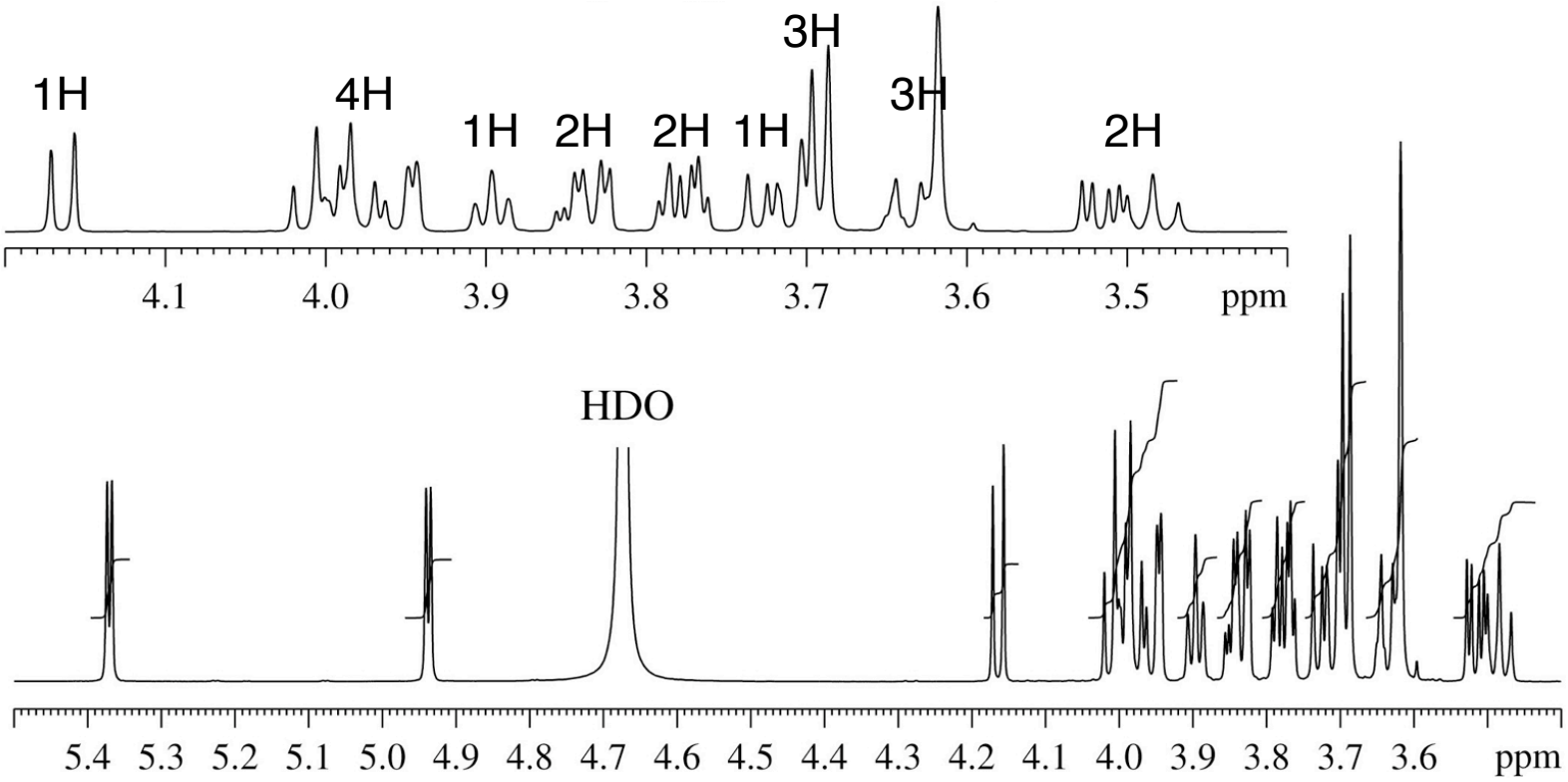
- Newer method is DQF (Double Quantum Filtered)-COSY
  - same information, but looks "cleaner"

2D NMR Spectroscopy

Who is Talking to Who?

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

– Overlapping protons and a lot of similar coupling constants



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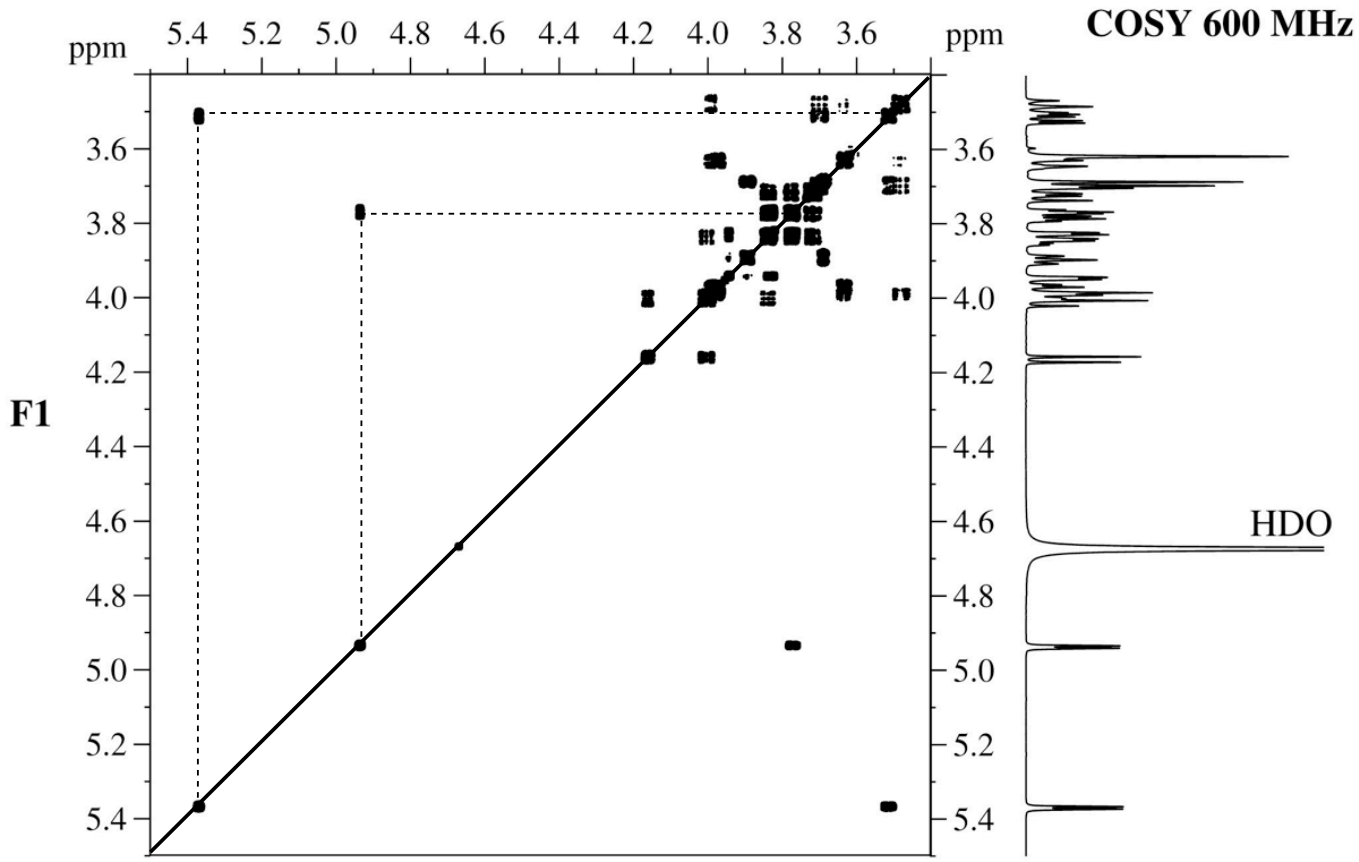

2D NMR Spectroscopy

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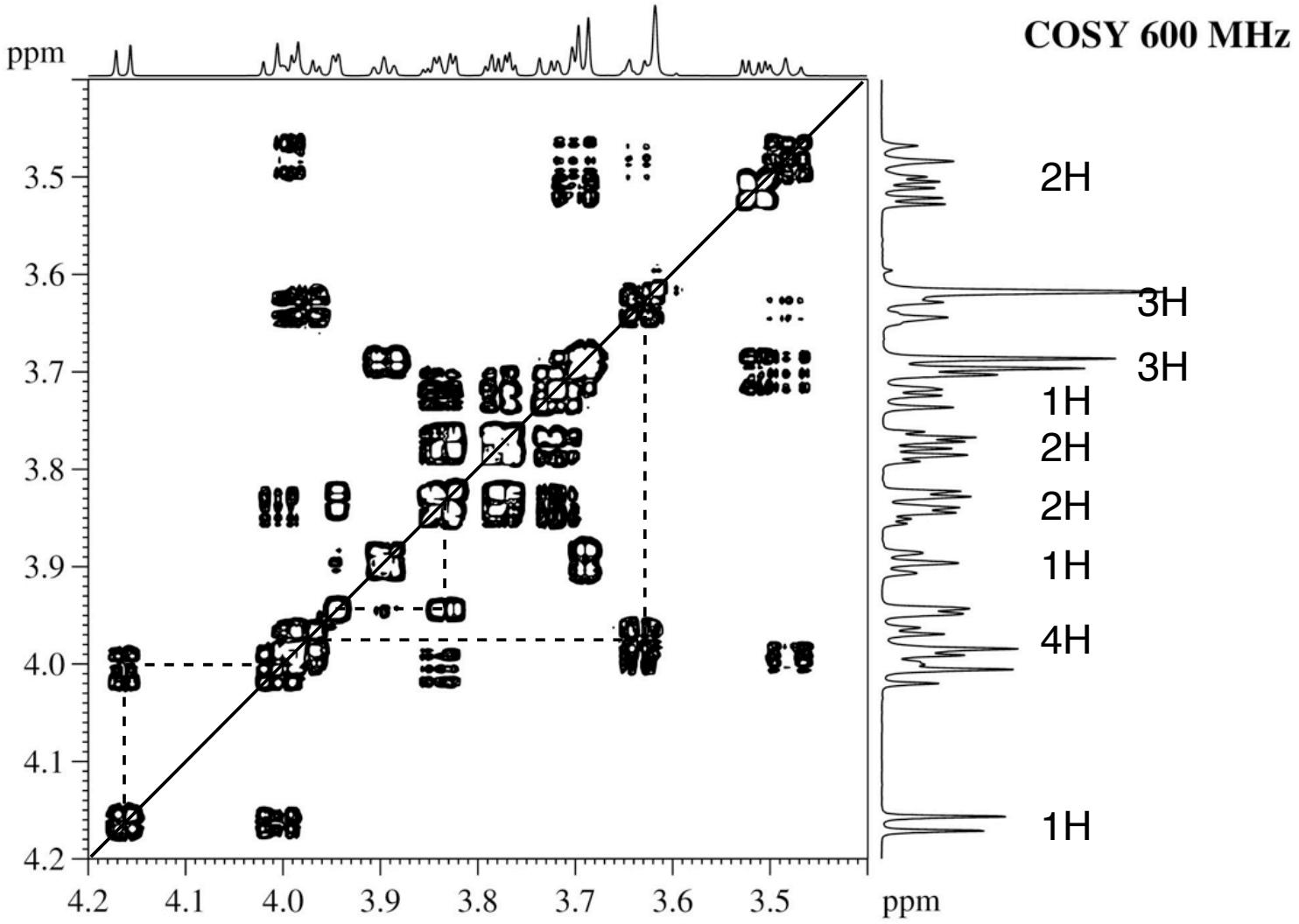
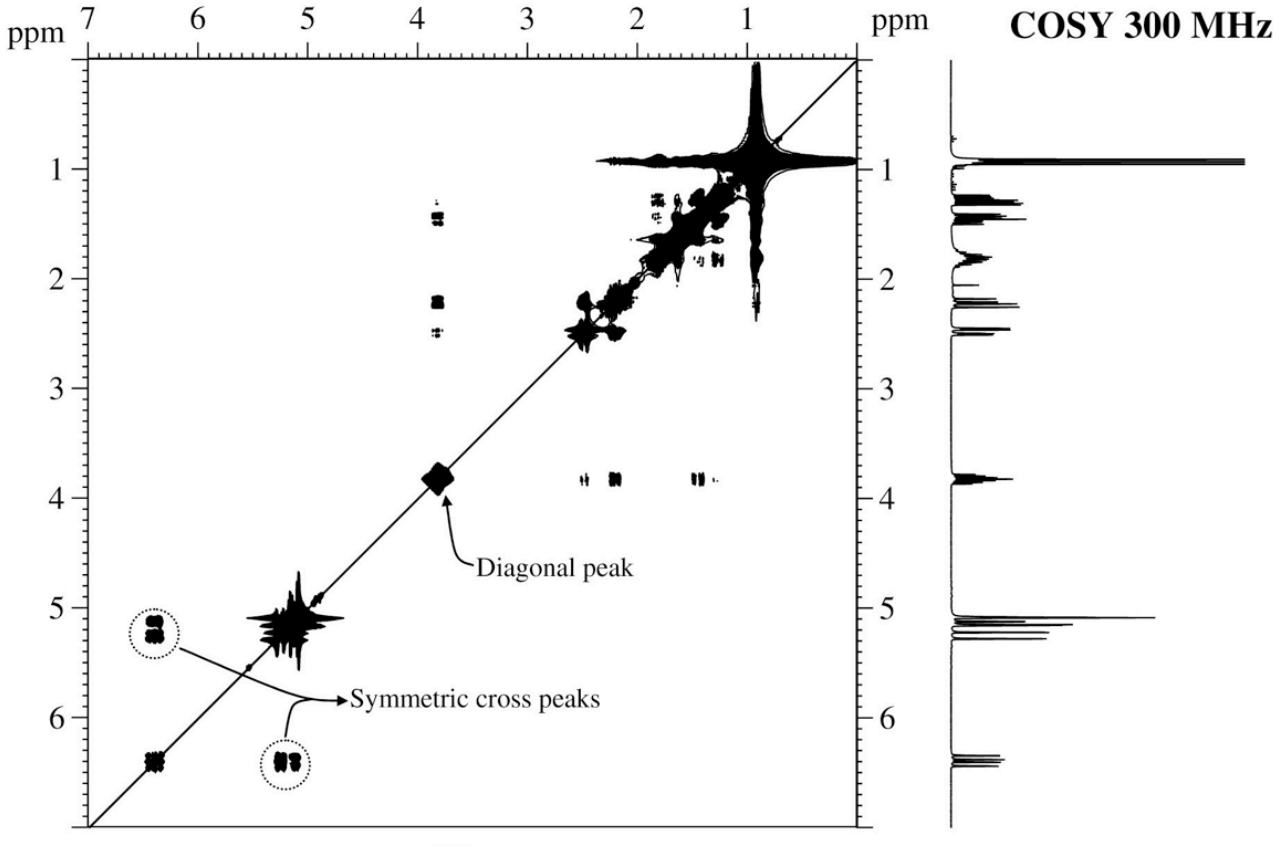


2D NMR Spectroscopy

Who is Talking to Who?

^{1}H–^{1}H COSY (*C*orrelation *S*pectroscopy)

– DQF-COSY: *D*ouble *Q*uantum *F*iltered COSY – cleans up the spectrum by reducing noncoupled systems (e.g. CH3 singlets)



2D NMR Spectroscopy

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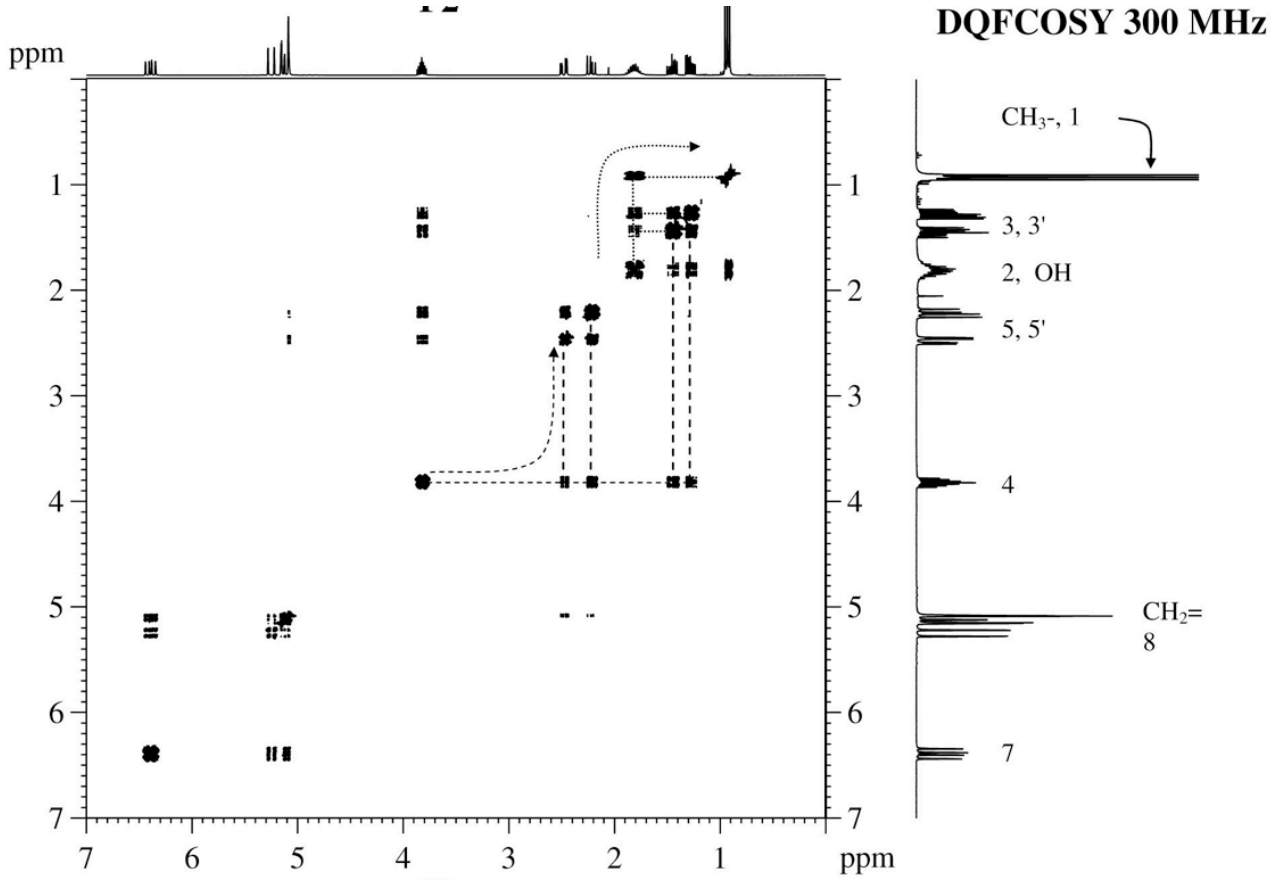
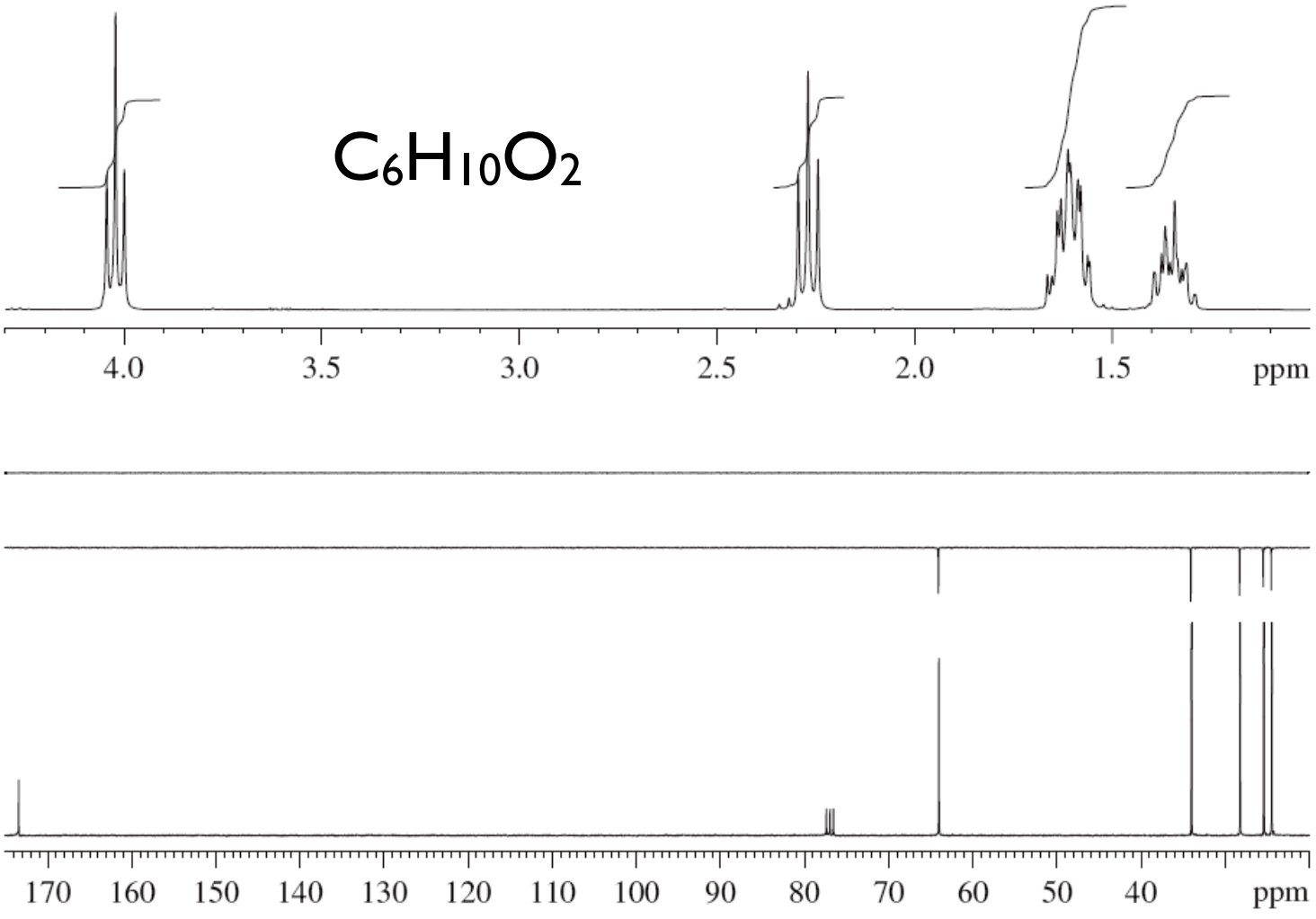


2D NMR Spectroscopy

Who is Talking to Who?

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

$C_6H_{10}O_2$



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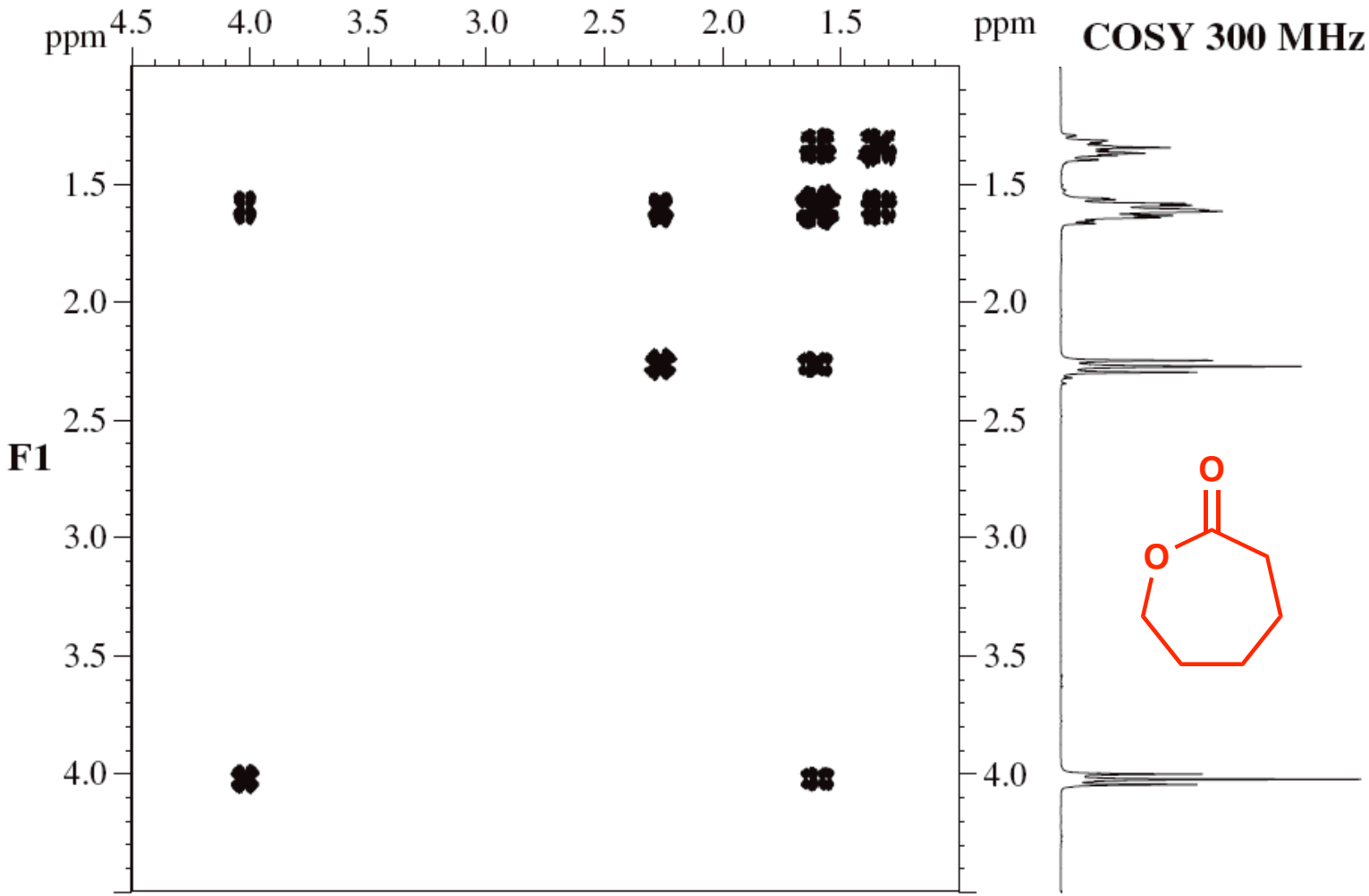
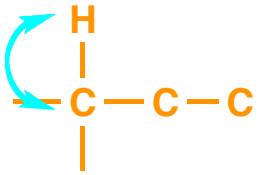


2D NMR Spectroscopy

Who is Talking to Who?

^{1}H–^{13}C COSY

- HETCOR (Heteronuclear Correlation)
  - older experiment; ^{13}C-detected
- HMQC (Heteronuclear Multiple Quantum Correlation)
  - newer experiment; ^{1}H-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

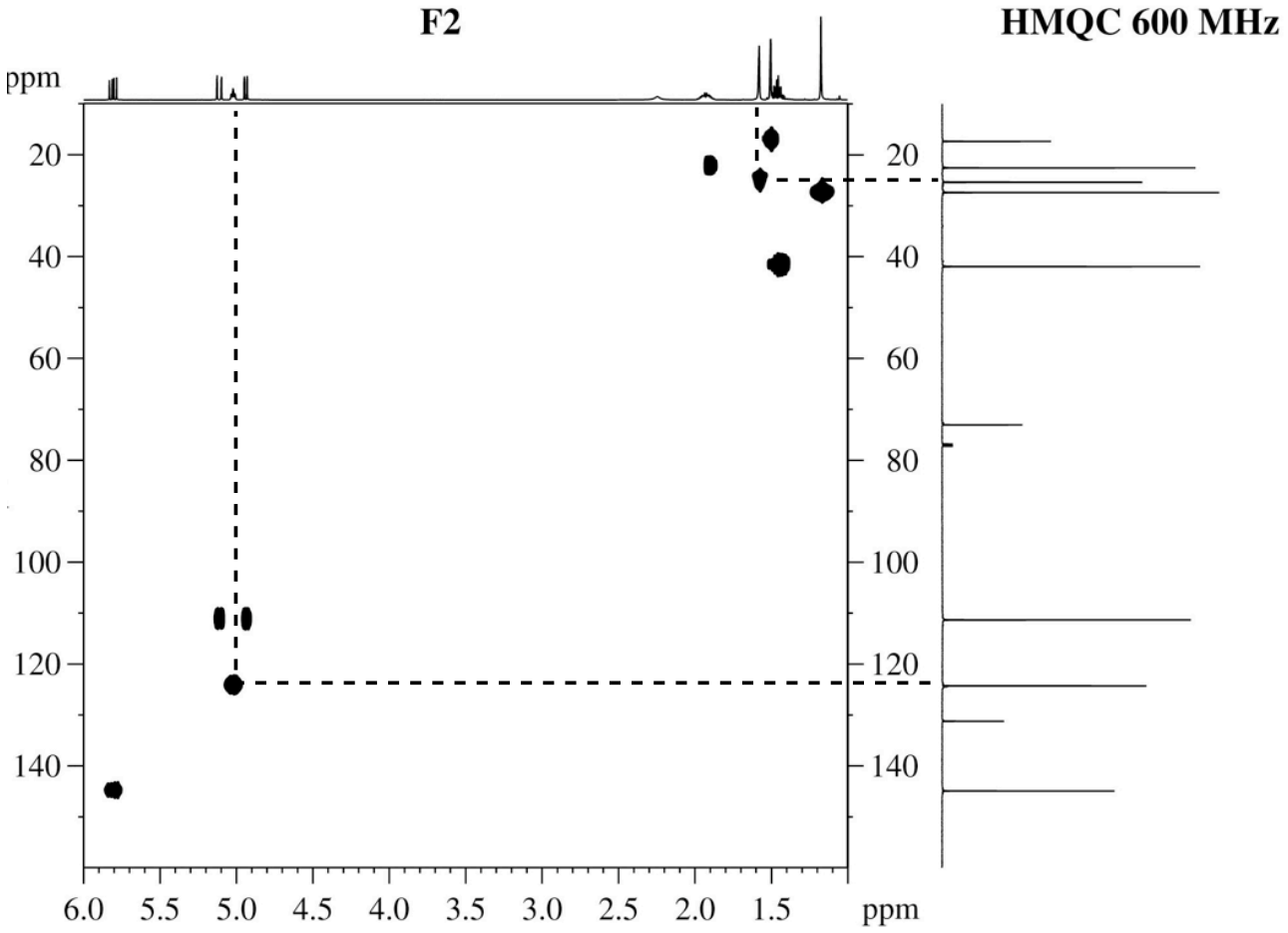


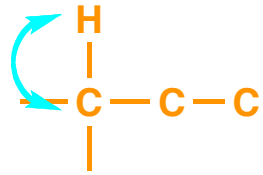
1 bond H–C coupling

2D NMR Spectroscopy

Who is Talking to Who?

HMQC





1 bond H–C coupling

2D NMR Spectroscopy

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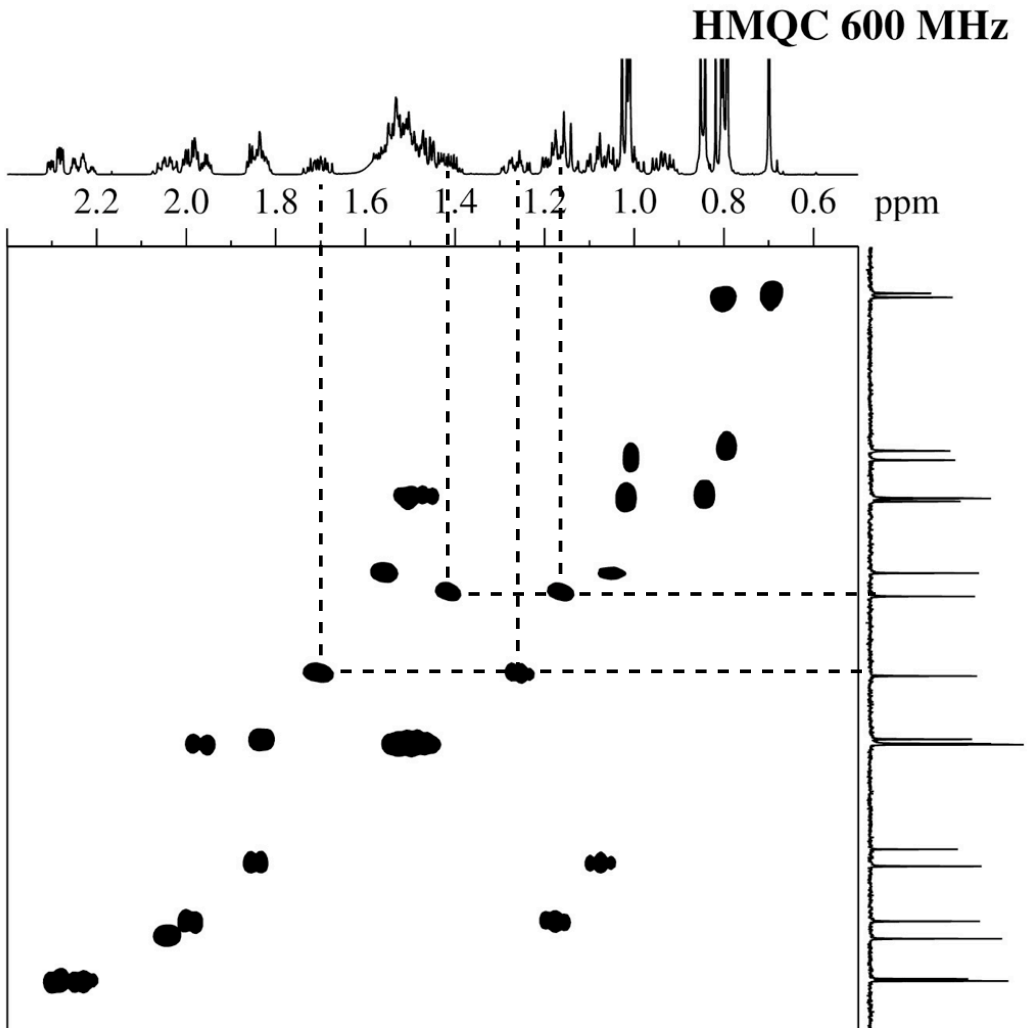
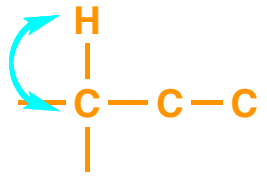
HMQC



Diastereotopic Protons



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2D NMR Spectroscopy

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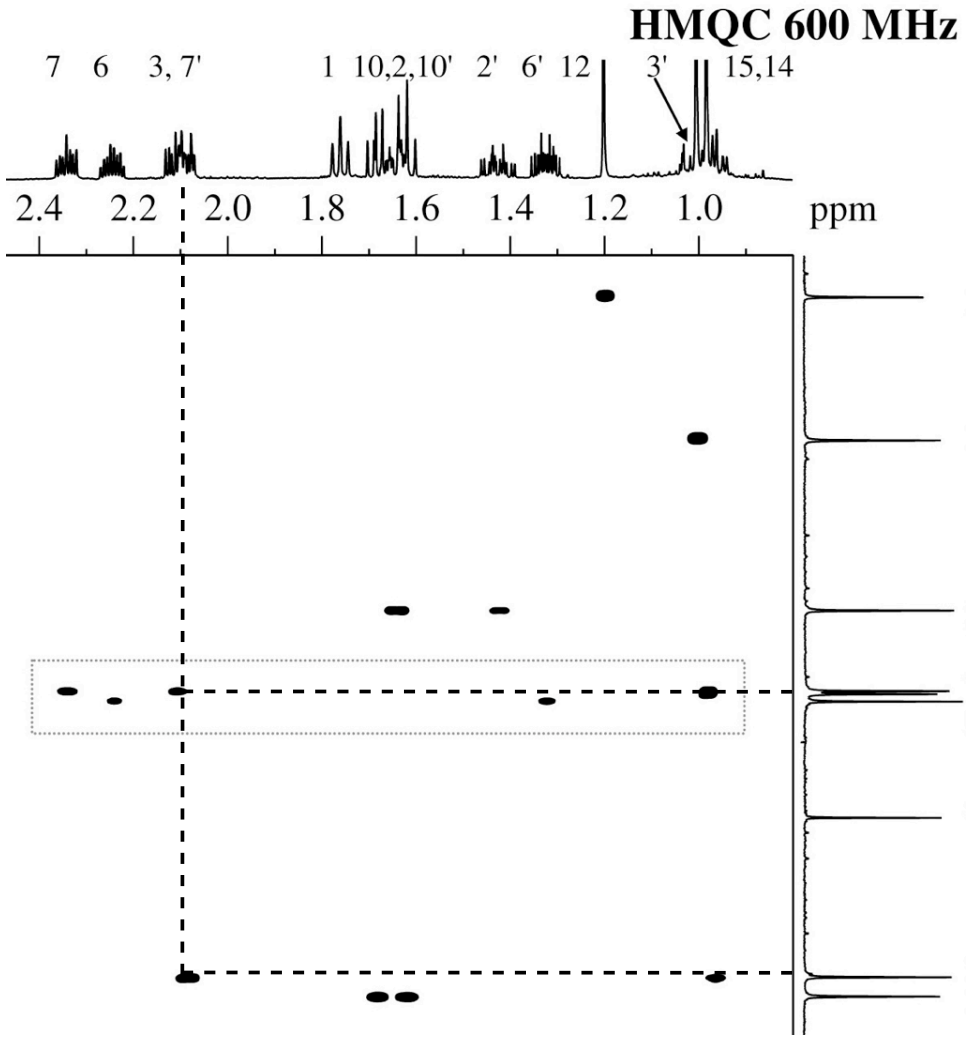
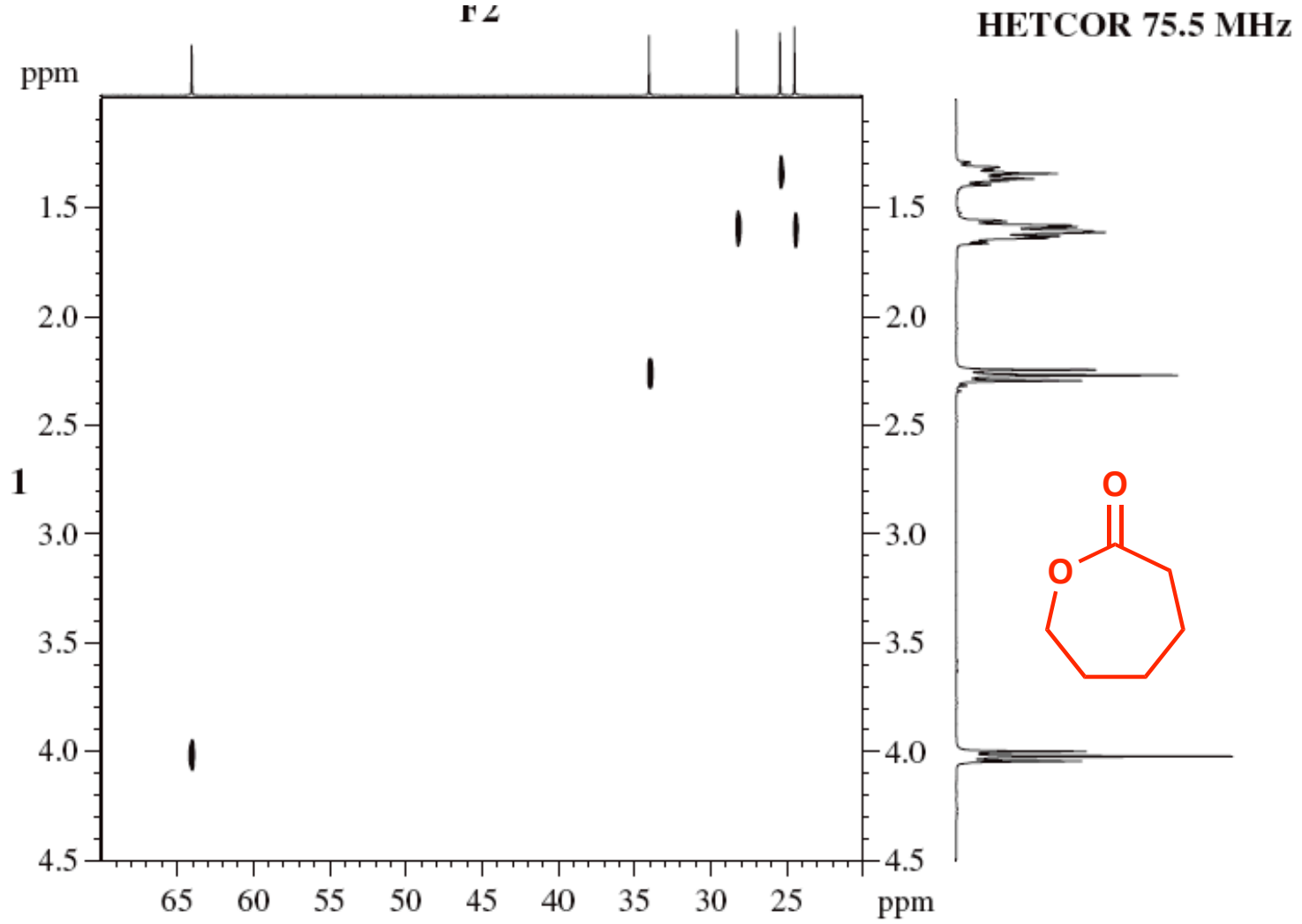


Can "see into" multiplets

2D NMR Spectroscopy

Who is Talking to Who?

HMQC



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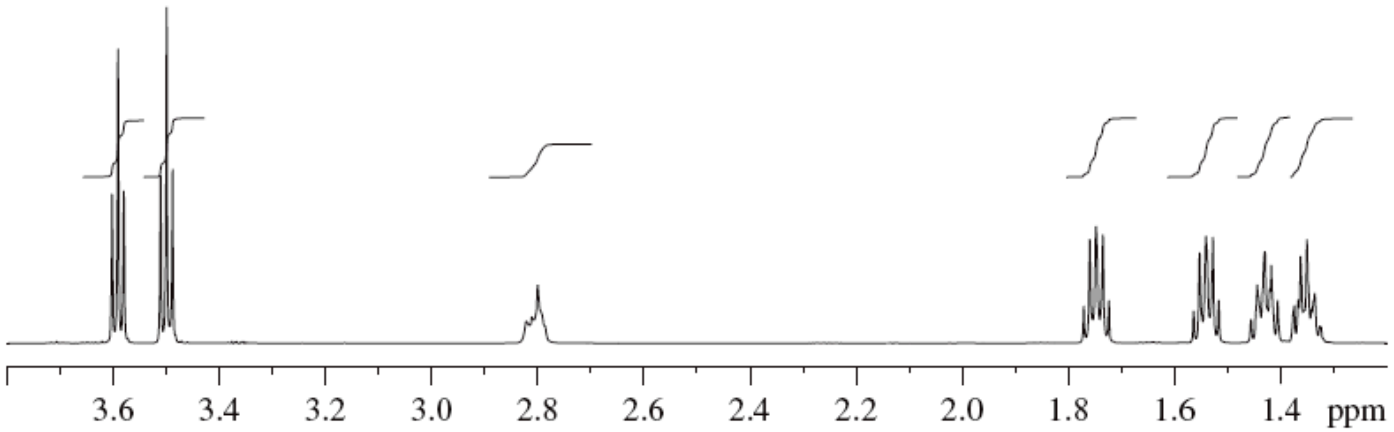
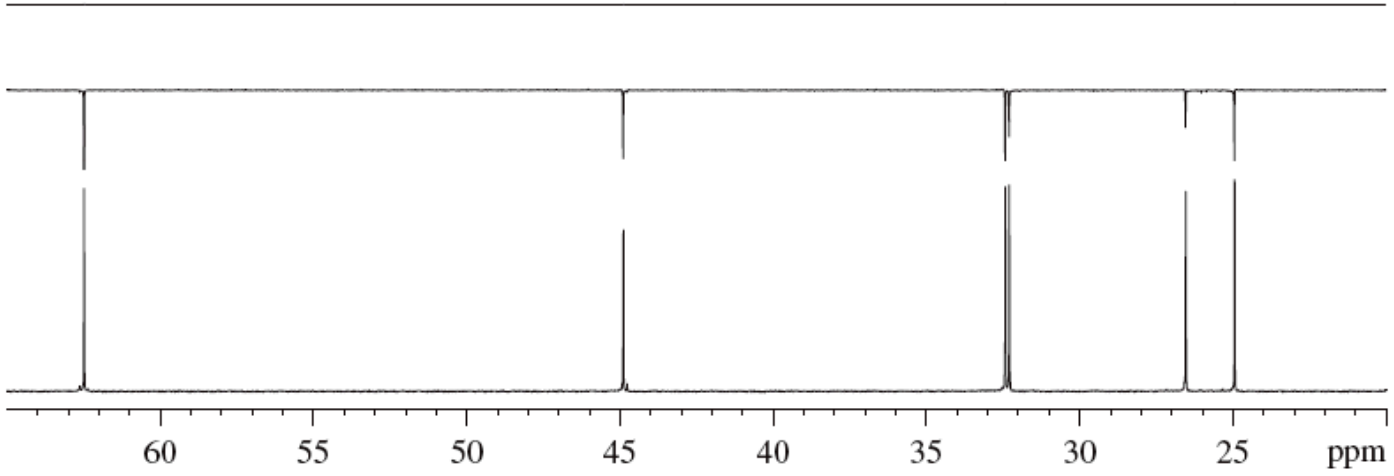


^{13}C/DEPT NMR 150.9 MHz



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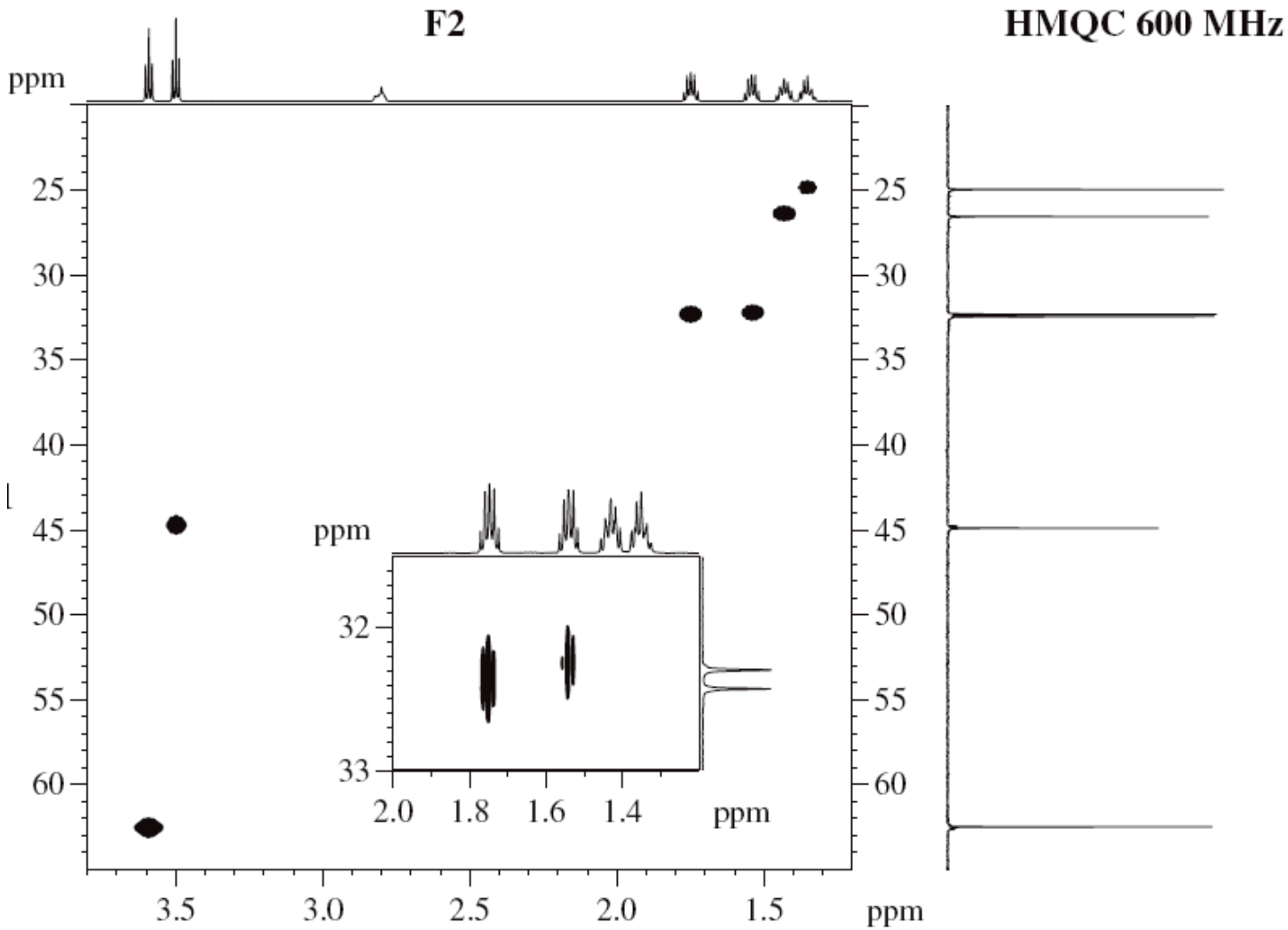

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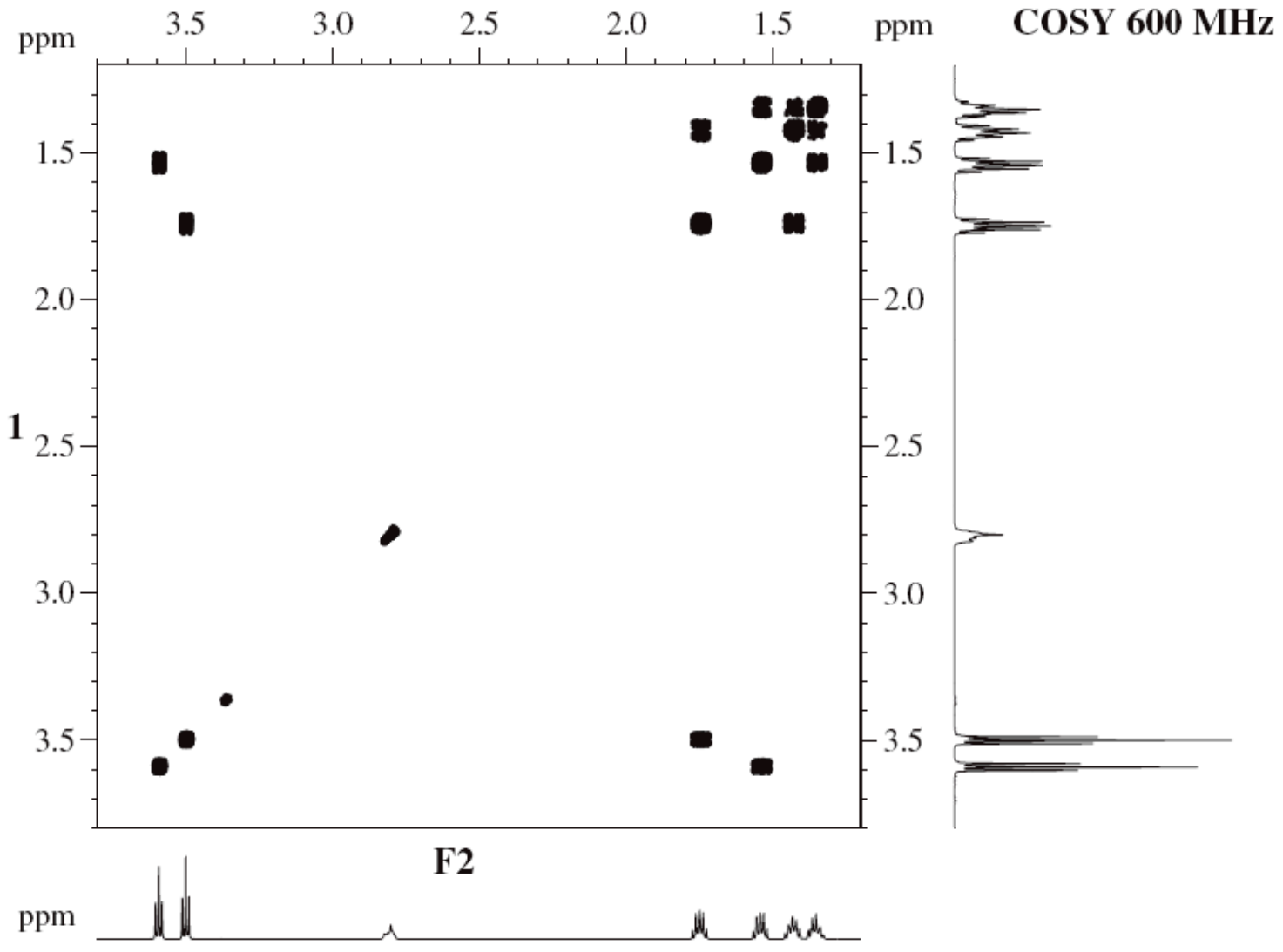
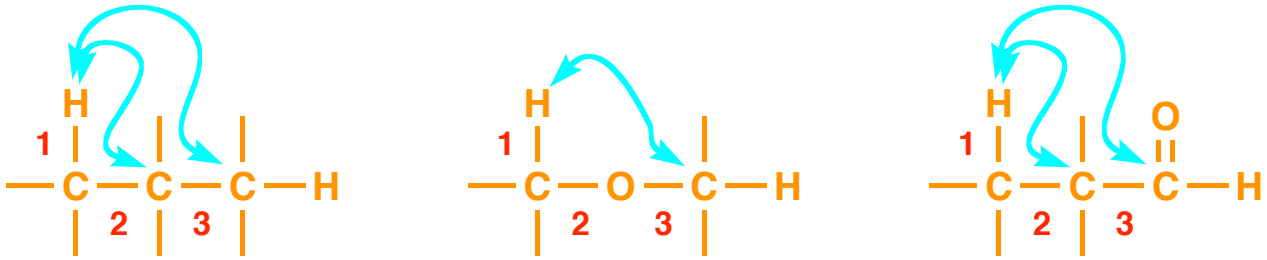


2D NMR Spectroscopy

Who is Talking to Who?

^{1}H–^{13}C COSY (Long Range)

- COLOC (Correlated spectroscopy for Long range Couplings)
  - older experiment; ^{13}C-detected
- HMBC (Heteronuclear Multiple Bond Coherence)
  - newer experiment; ^{1}H-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

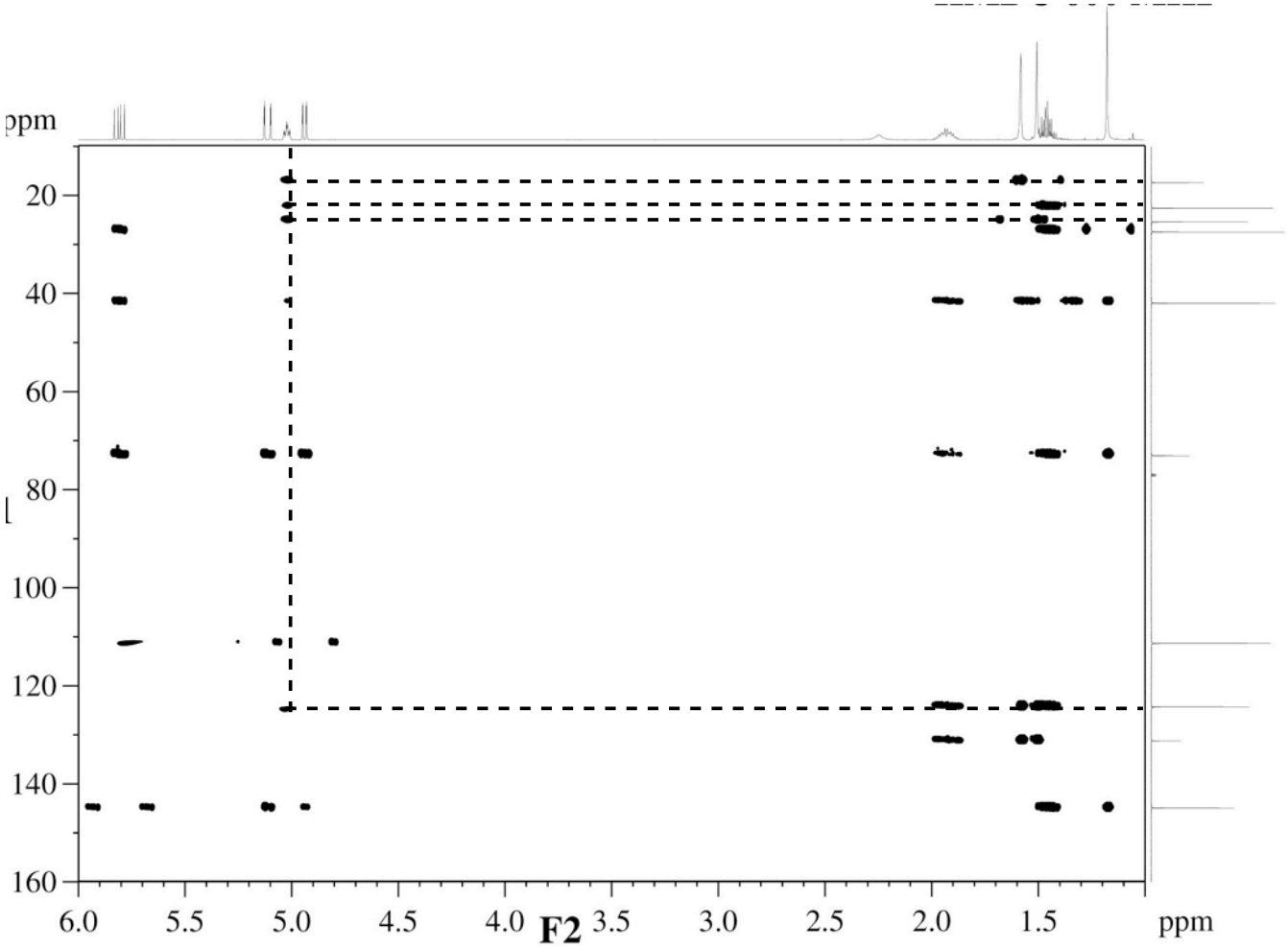


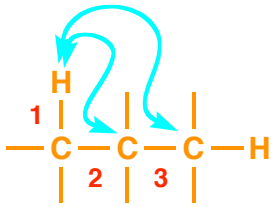
2 and 3 bond H–C couplings

2D NMR Spectroscopy

Who is Talking to Who?

HMBC





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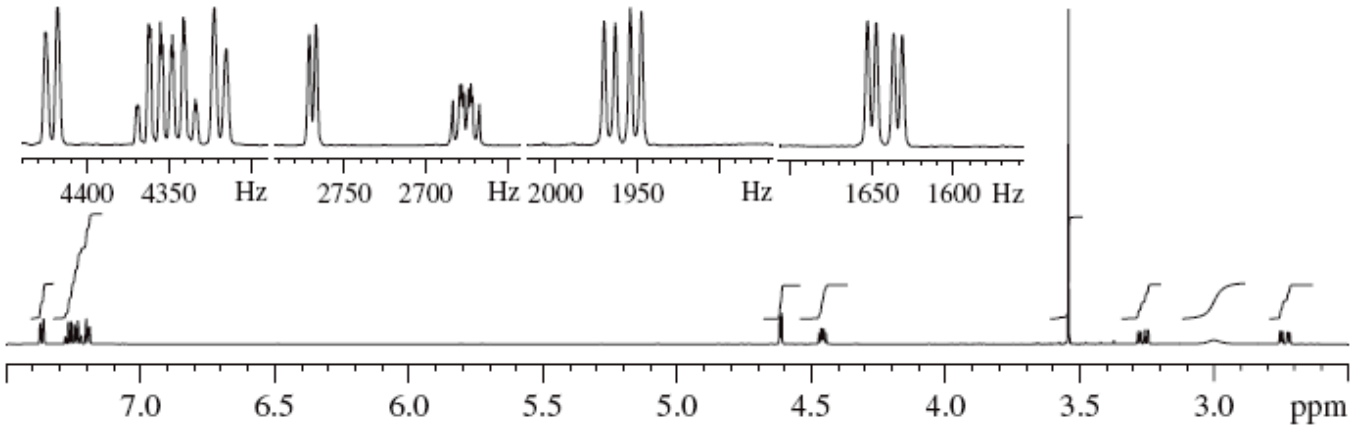
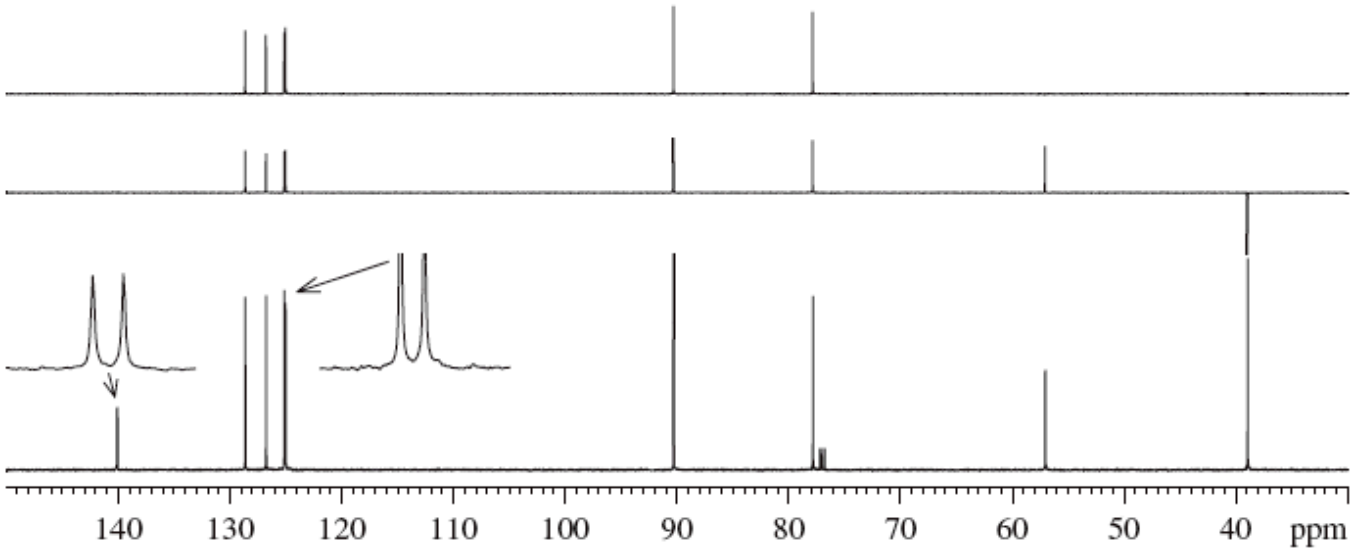


^{13}C/DEPT NMR 150.9 MHz



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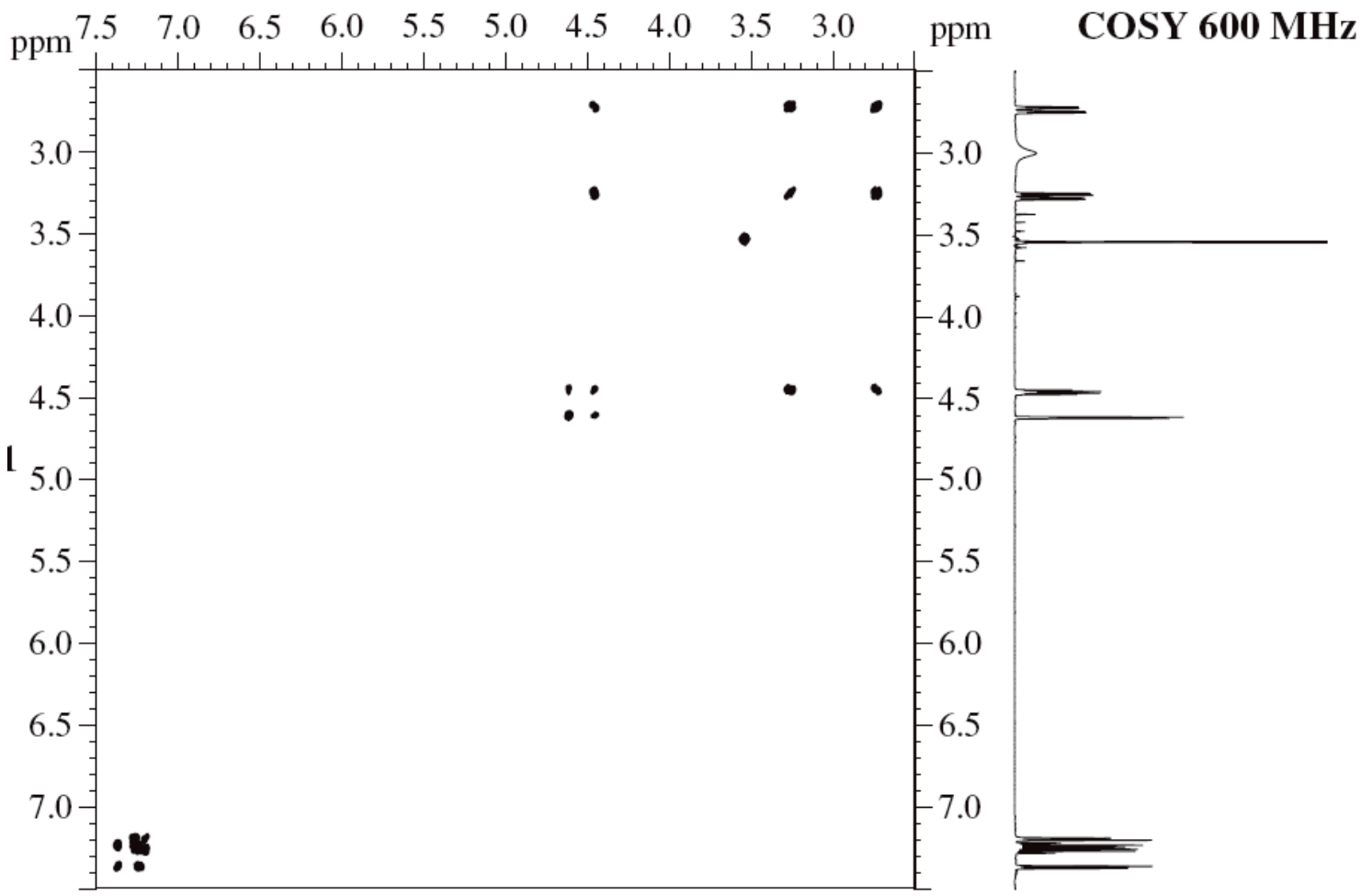

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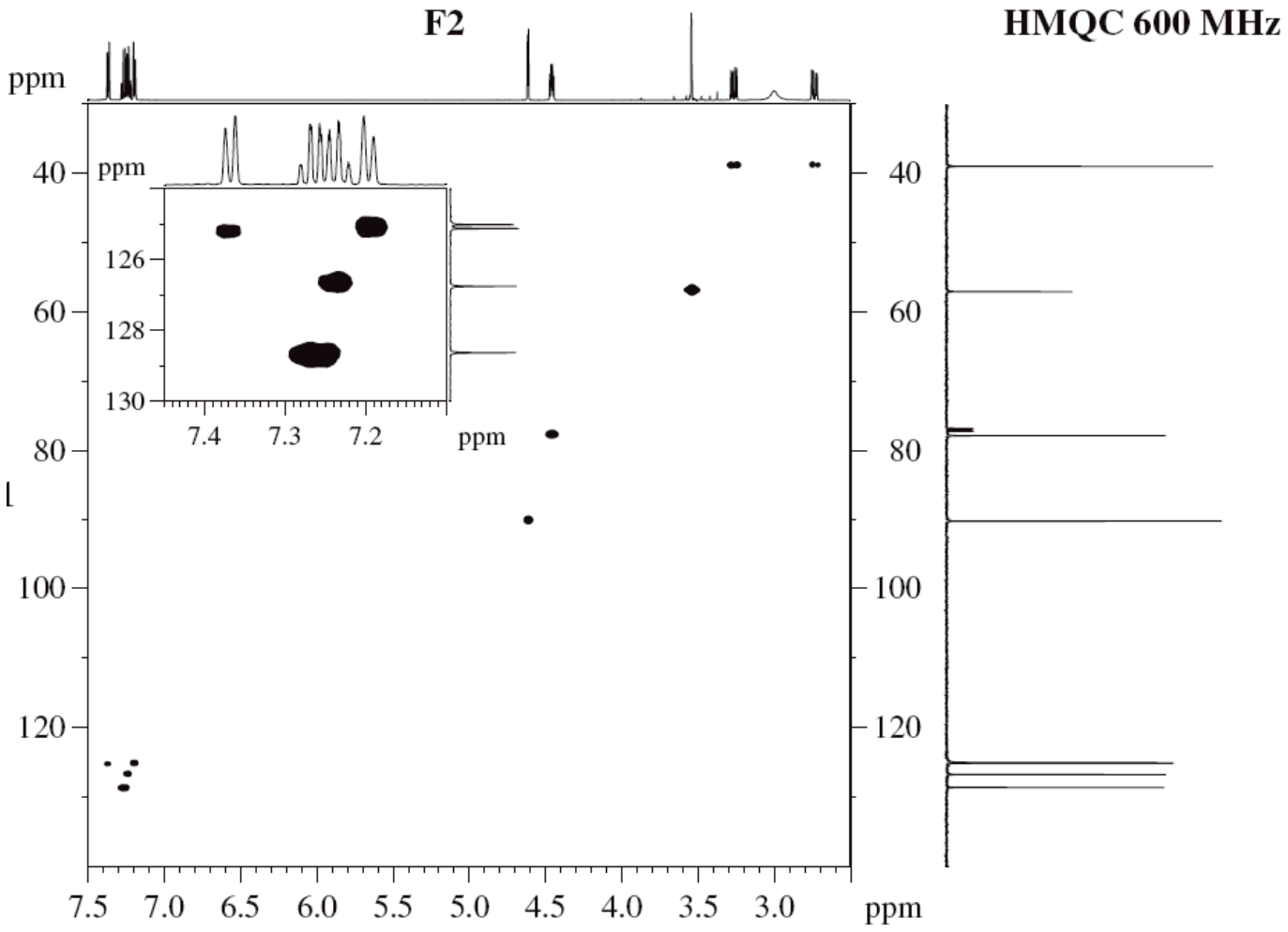

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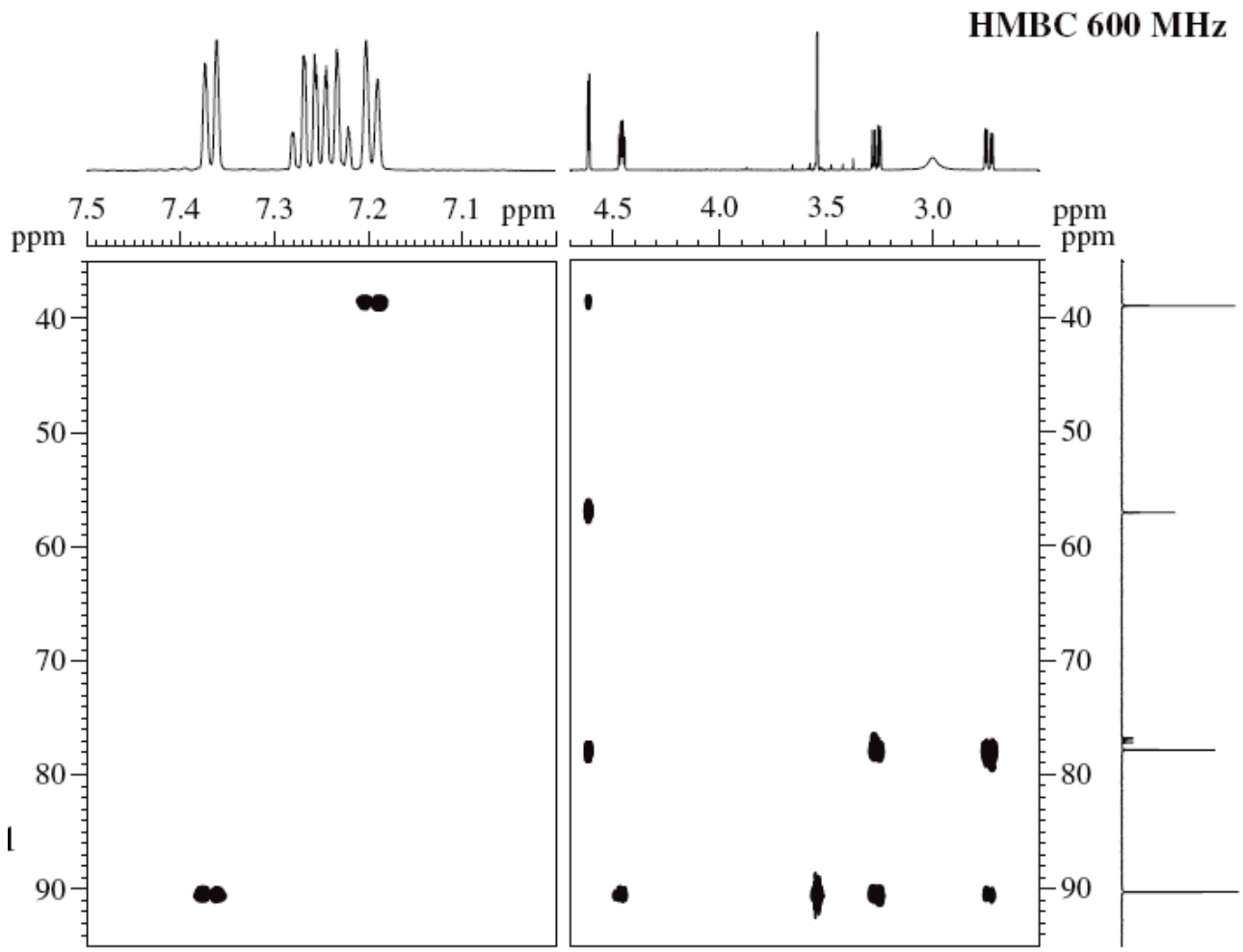

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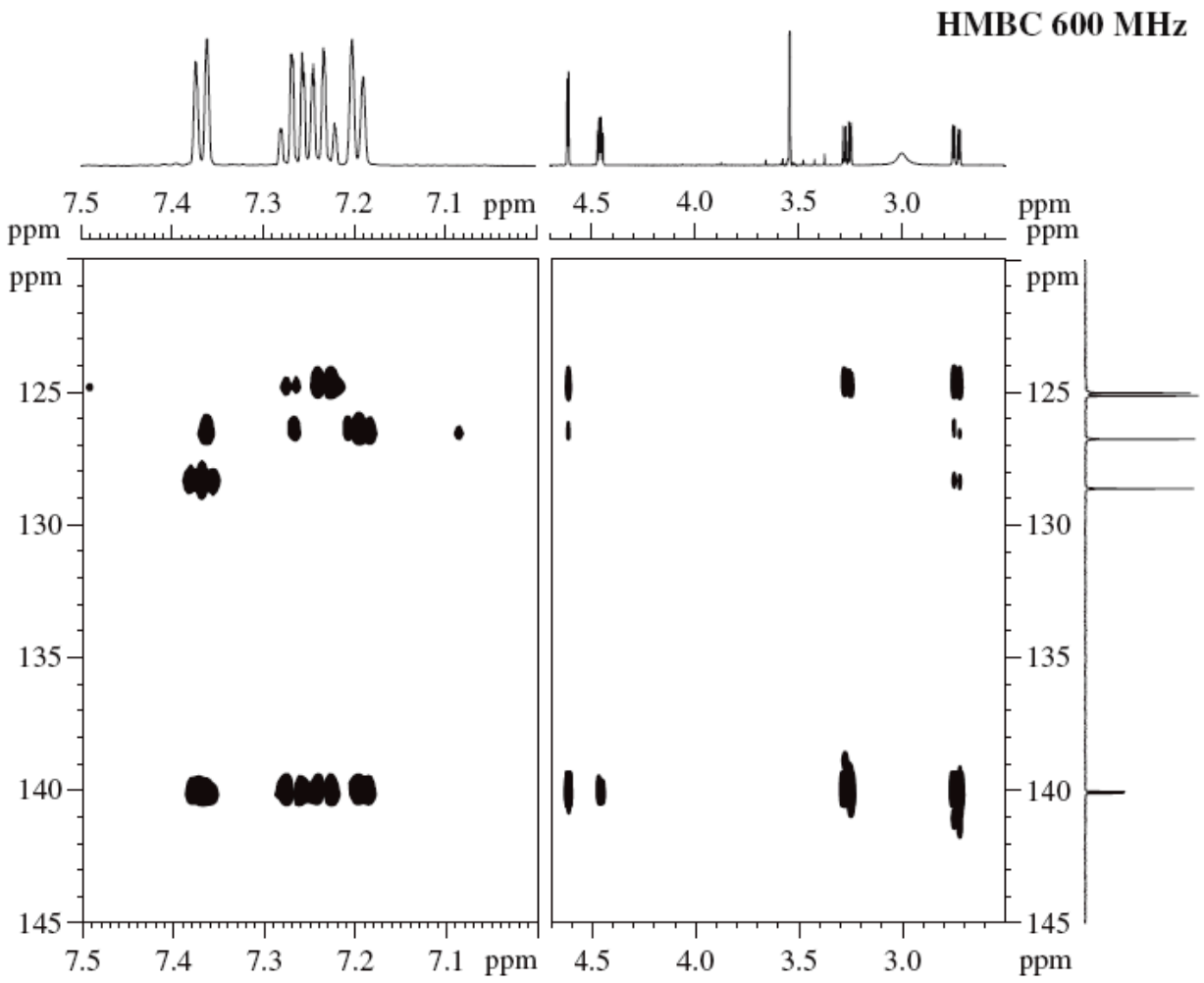
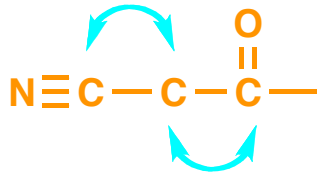


2D NMR Spectroscopy

Who is Talking to Who?

^{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, CH_2, CH_3, 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 0.01x0.01 = 0.0001 (~1 molecule in 10,000)



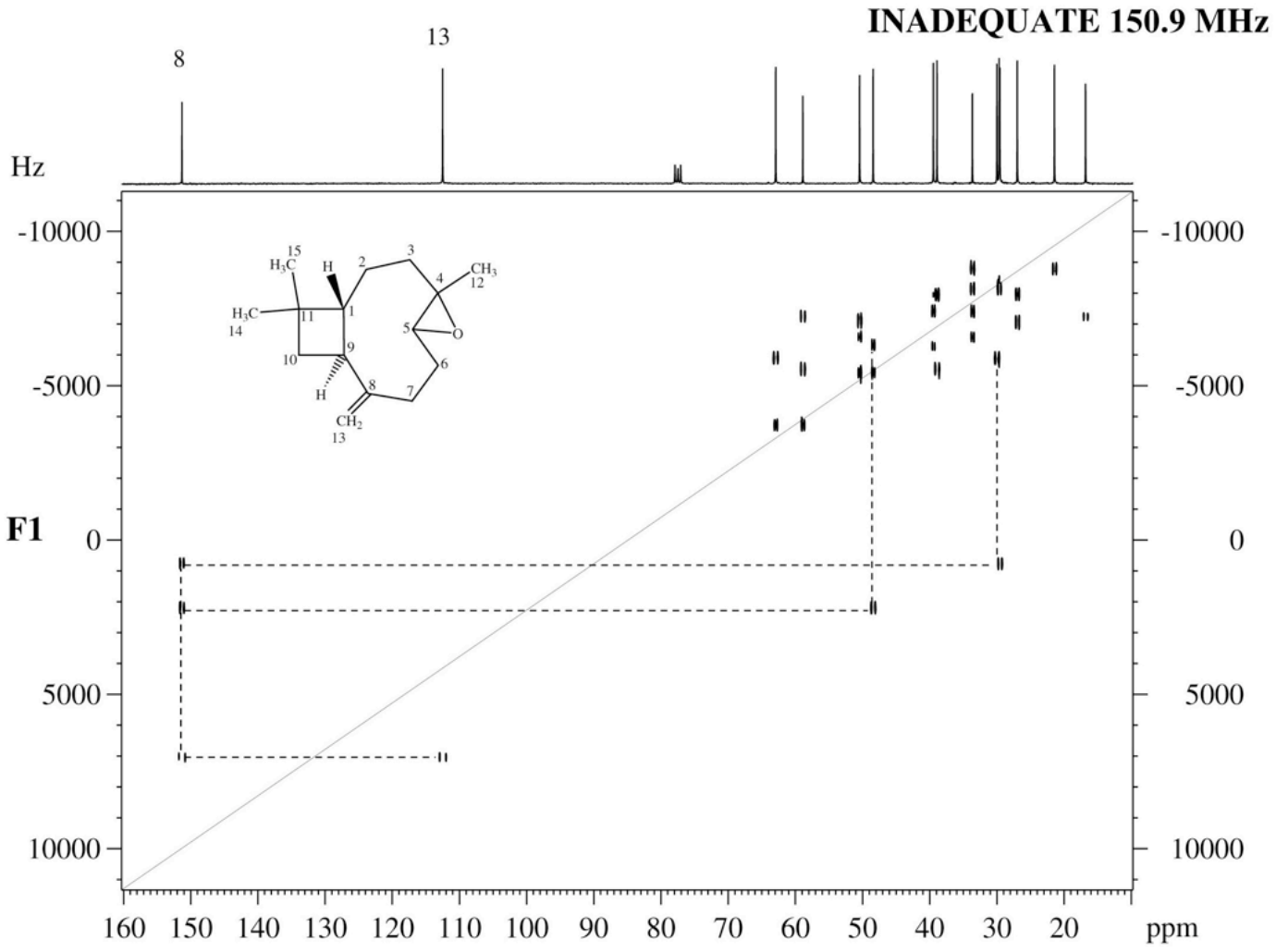
1 bond C–C coupling

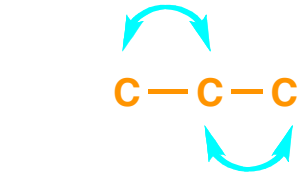
- Need lots of sample and instrument time to overcome
- In our facility: 80% v/v, overnight, 500 MHz = nothing

2D NMR Spectroscopy

Who is Talking to Who?

INADEQUATE





1 bond C–C coupling

2D NMR Spectroscopy

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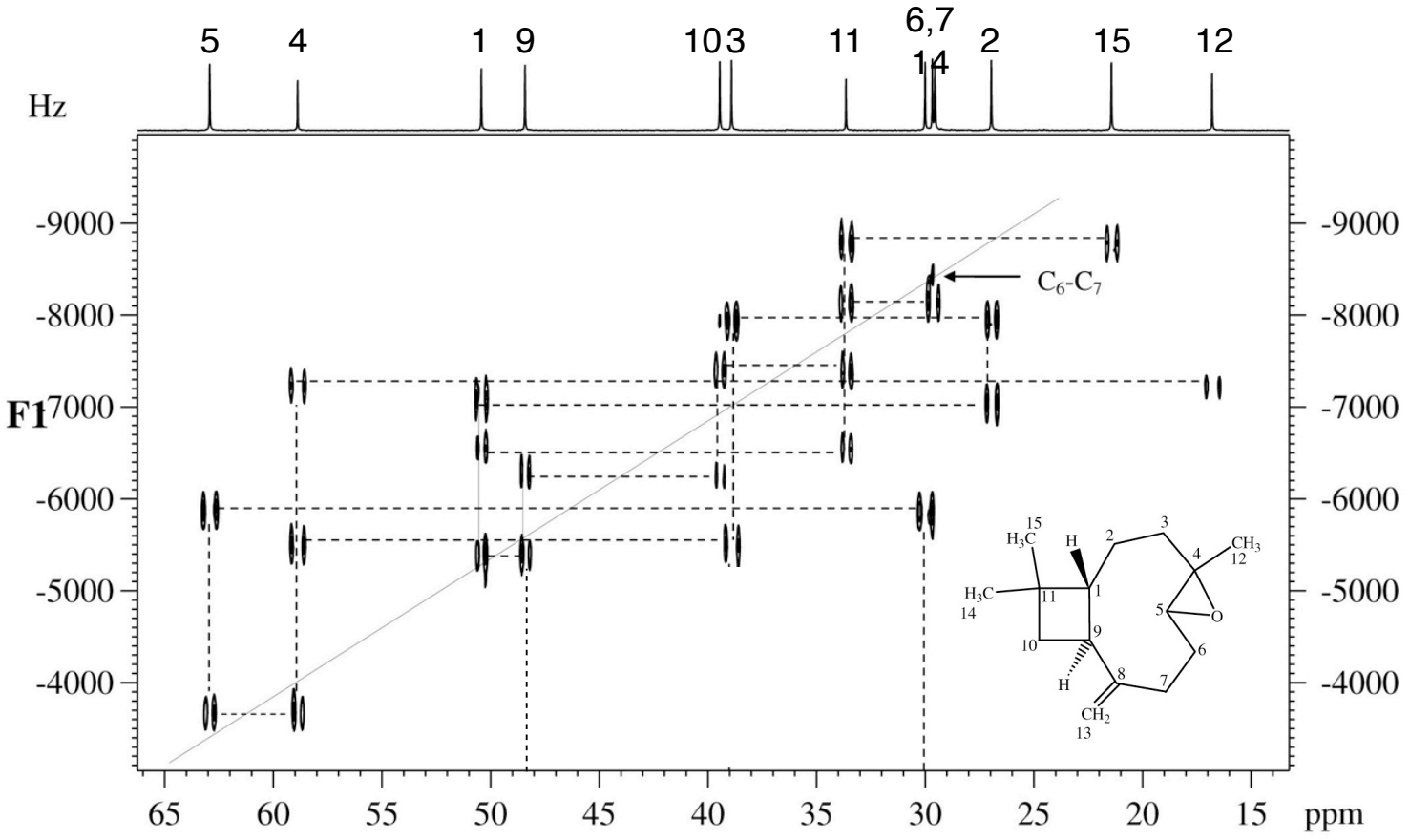
INADEQUATE

– Cross peaks show up as doublets = J_{CC}

– Diagonal is midway between the two doublets



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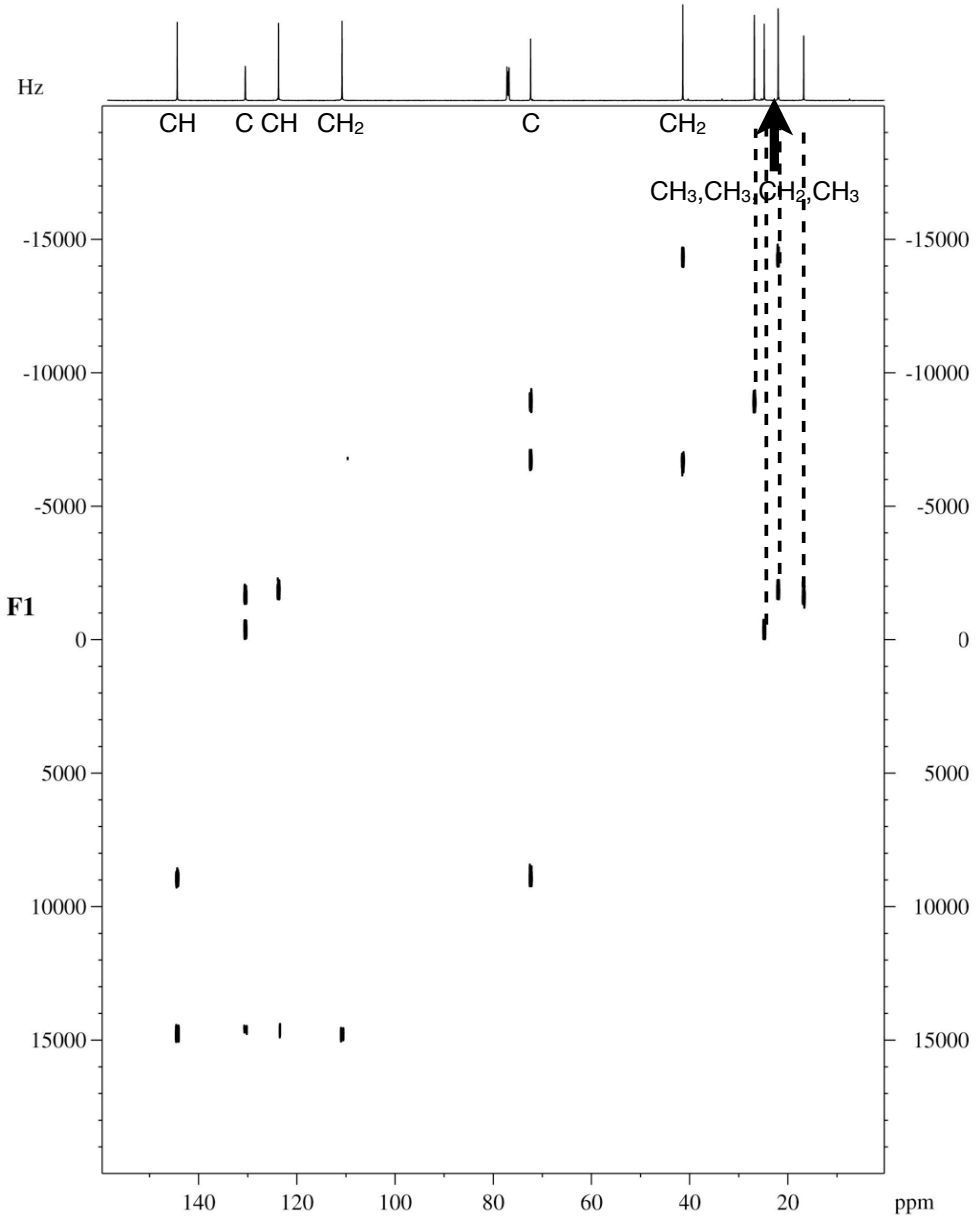

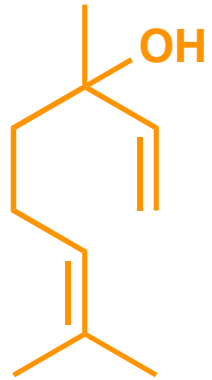

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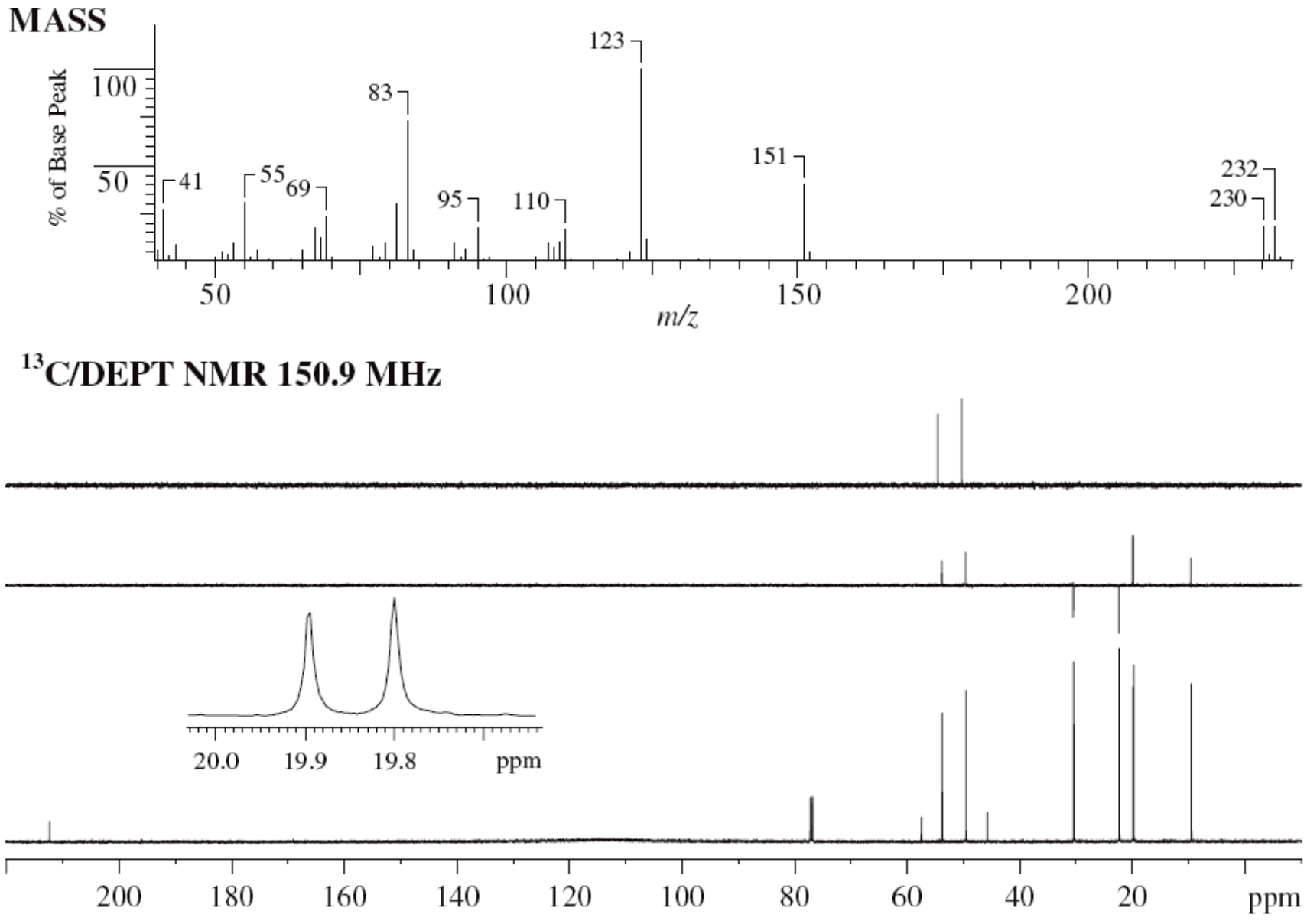

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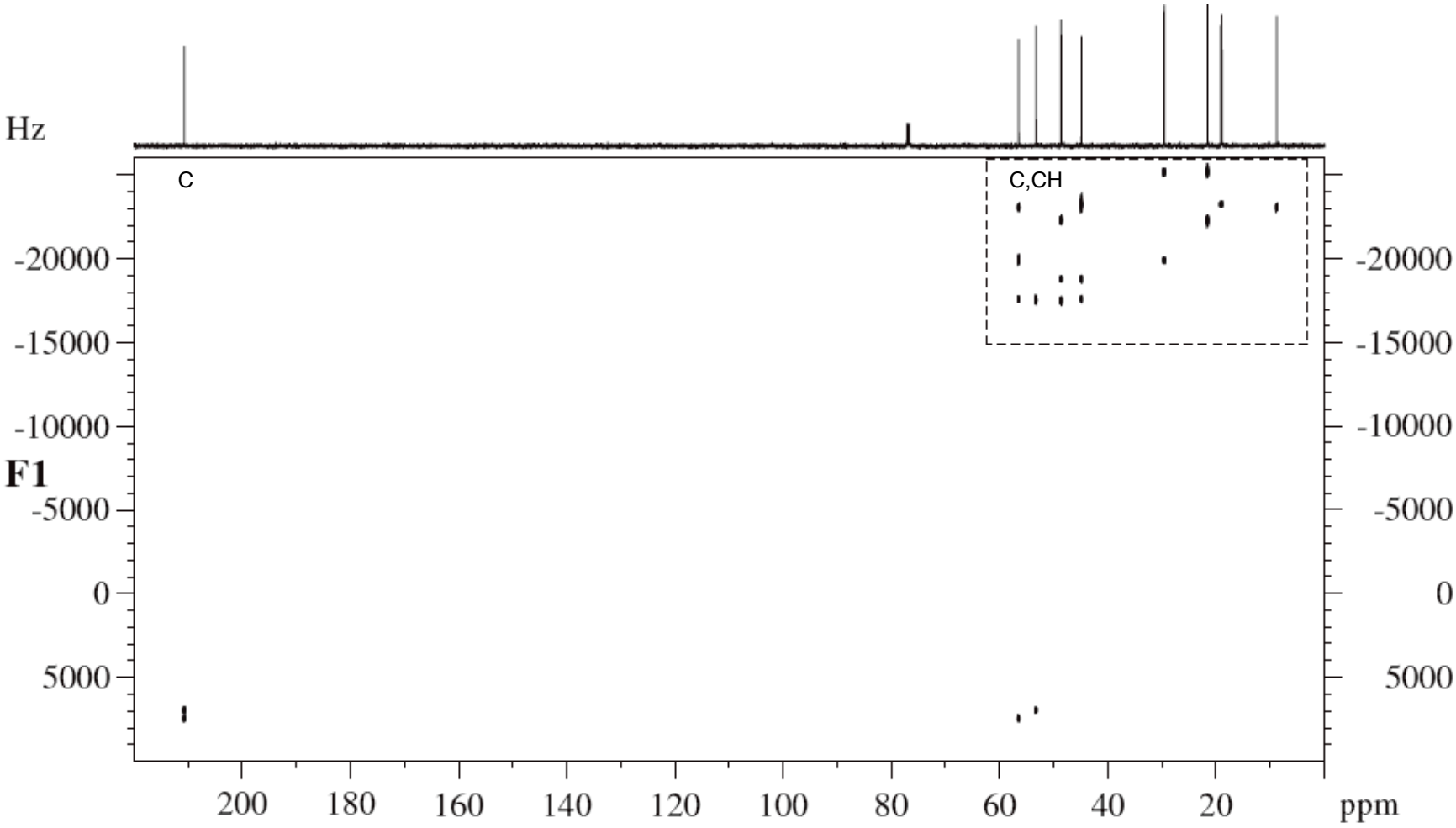

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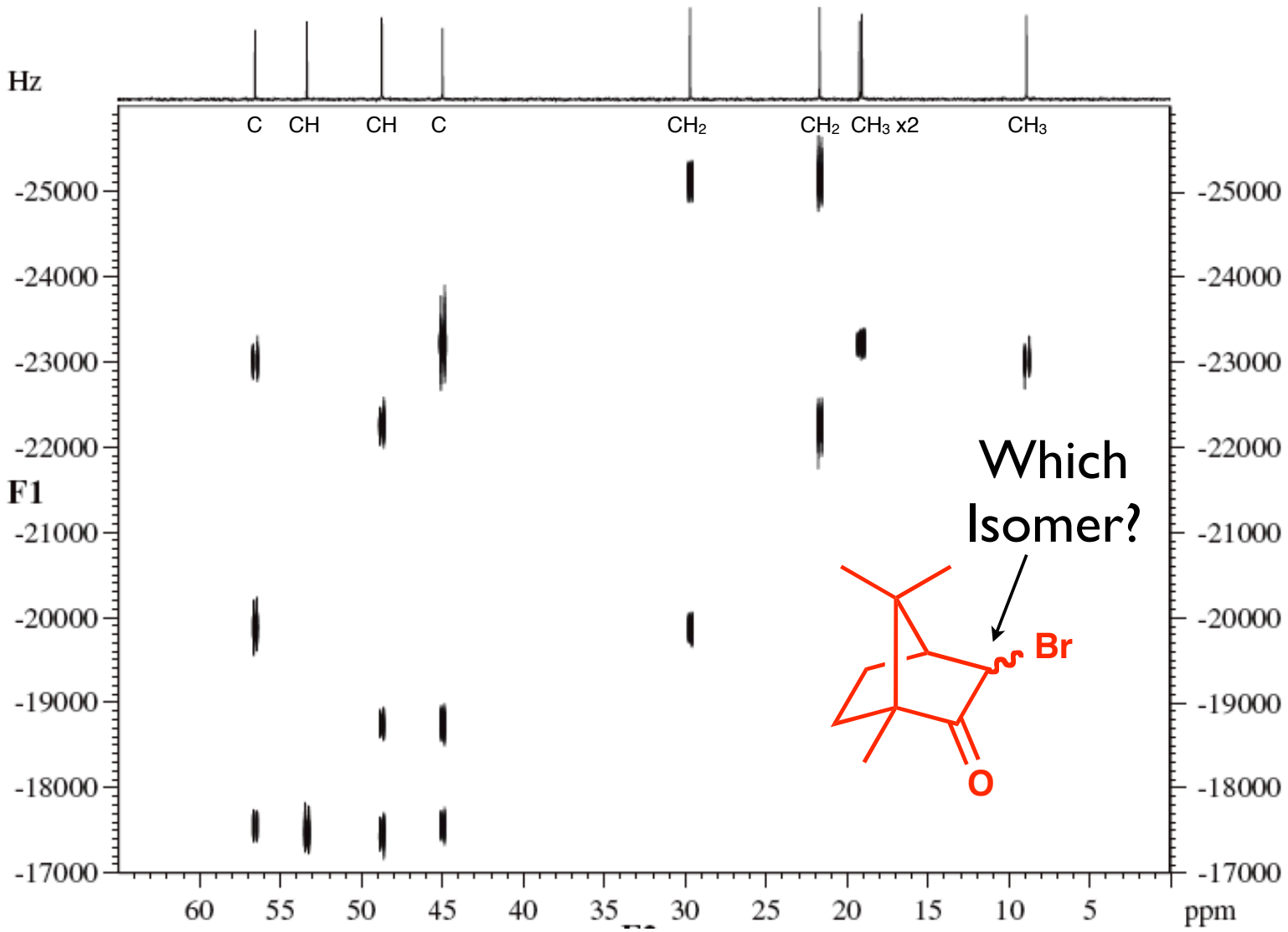

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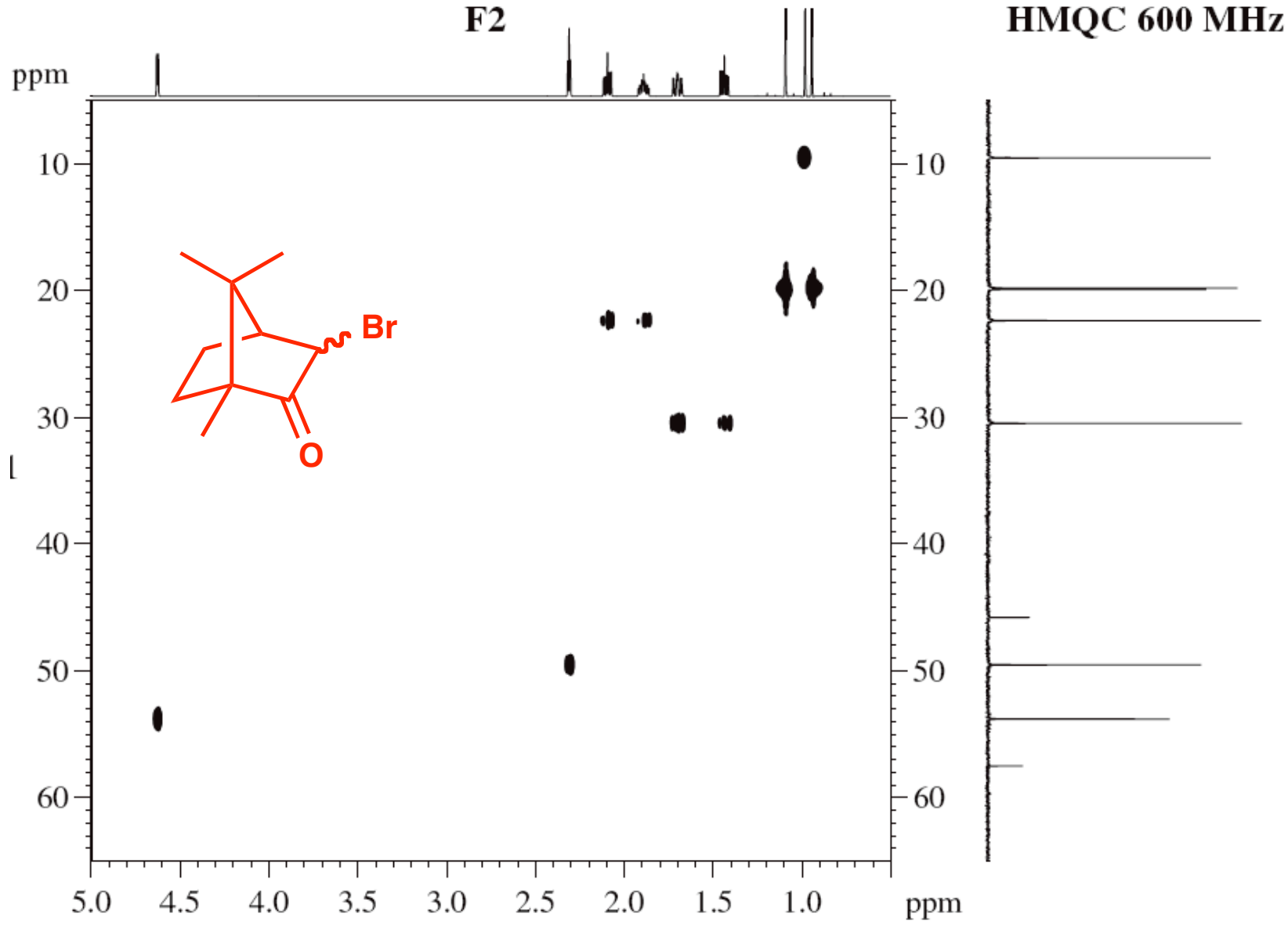

2D NMR Spectroscopy