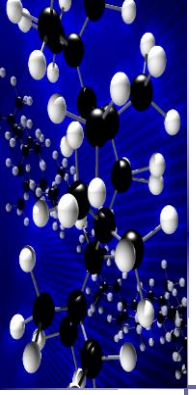


What NMR Can Do for You

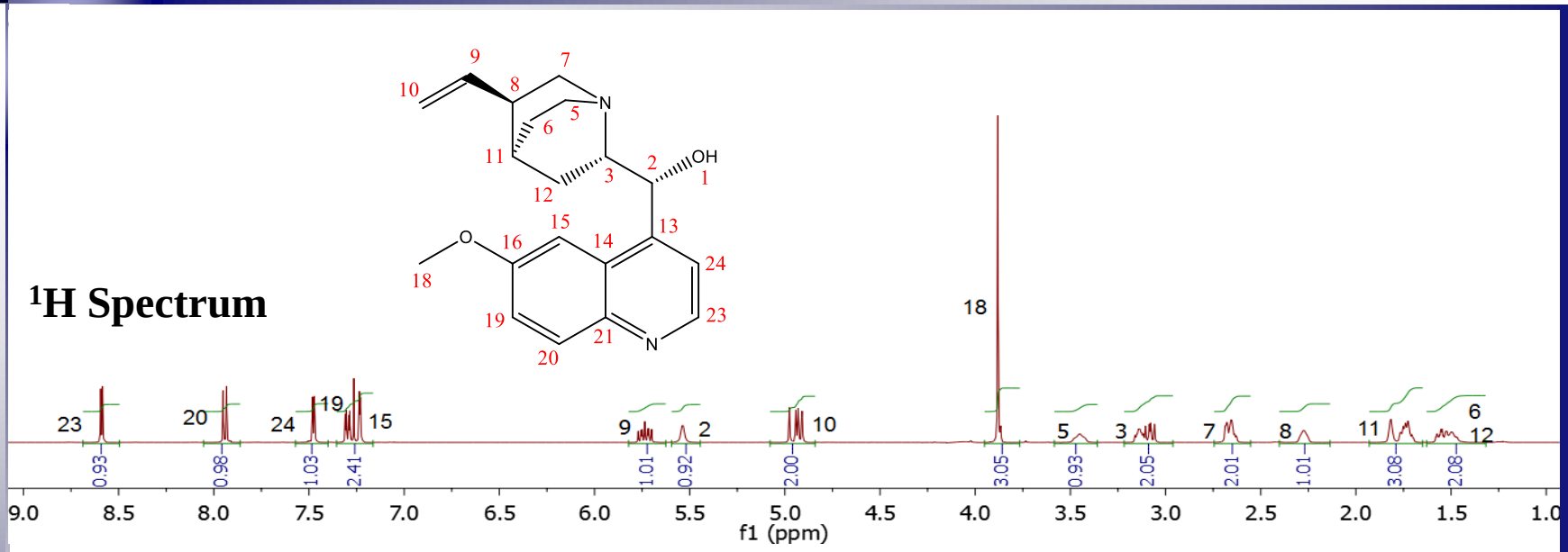
by Lingyang Zhu

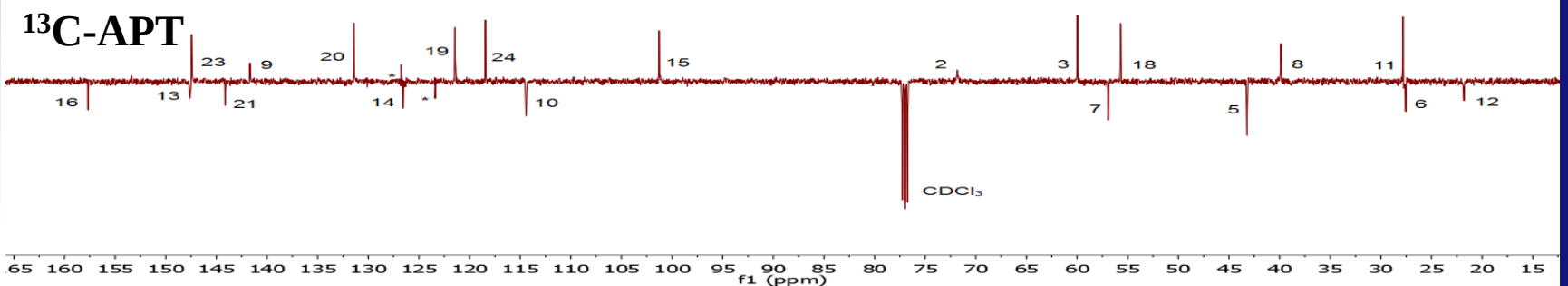
NMR Lab Overview

- **Structure Elucidation of Small Molecules**
  - Structure identification of synthetic compounds, intermediates, impurities, mixtures, unknowns, regiochemistry, rotamerization
  - Quantitative NMR
  - Chemical exchange: Equilibrium or A(Di)ssociation constants
  - Reaction monitoring or reaction rates
  - Diffusion coefficients (DOSY NMR): monomer? dimer?
  - Enantiomeric purity determination
  - Absolute stereochemistry determination
  - Dynamics (T_1, T_2 and NOE)
  - Intramolecular hydrogen-bond determination
  - Parahydrogen-NMR (enhance NMR signals thousands fold) to study reaction pathways
- **NMR Screening (Protein-Ligand Interaction)**
- **Structure and Dynamics of Macromolecules and Complexes (e.g., peptides and proteins)**
- **Metabolites Analysis**

Count the Numbers

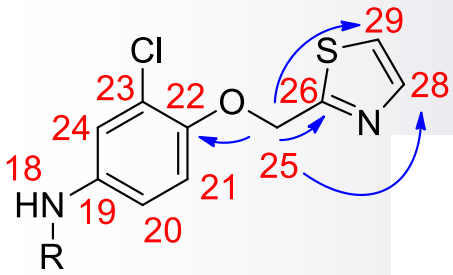
Solution NMR in Organic Chemistry
Research Examples

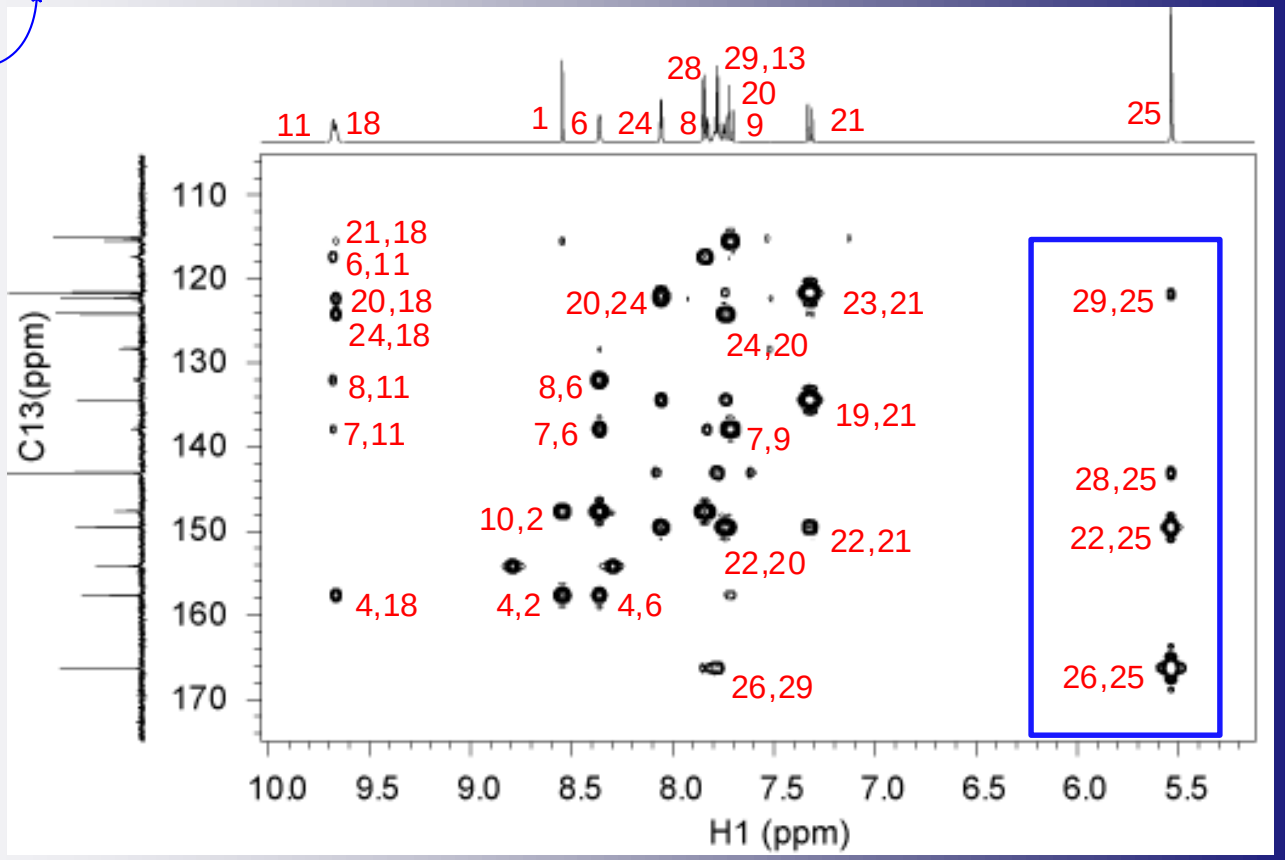




Long-Range Connectivity: ^{1}H-^{13}C gHMBC Spectrum

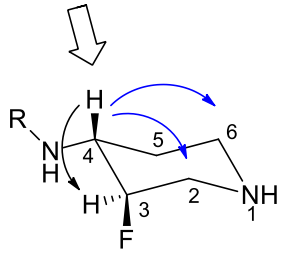
Solution NMR in Organic Chemistry
Research Examples

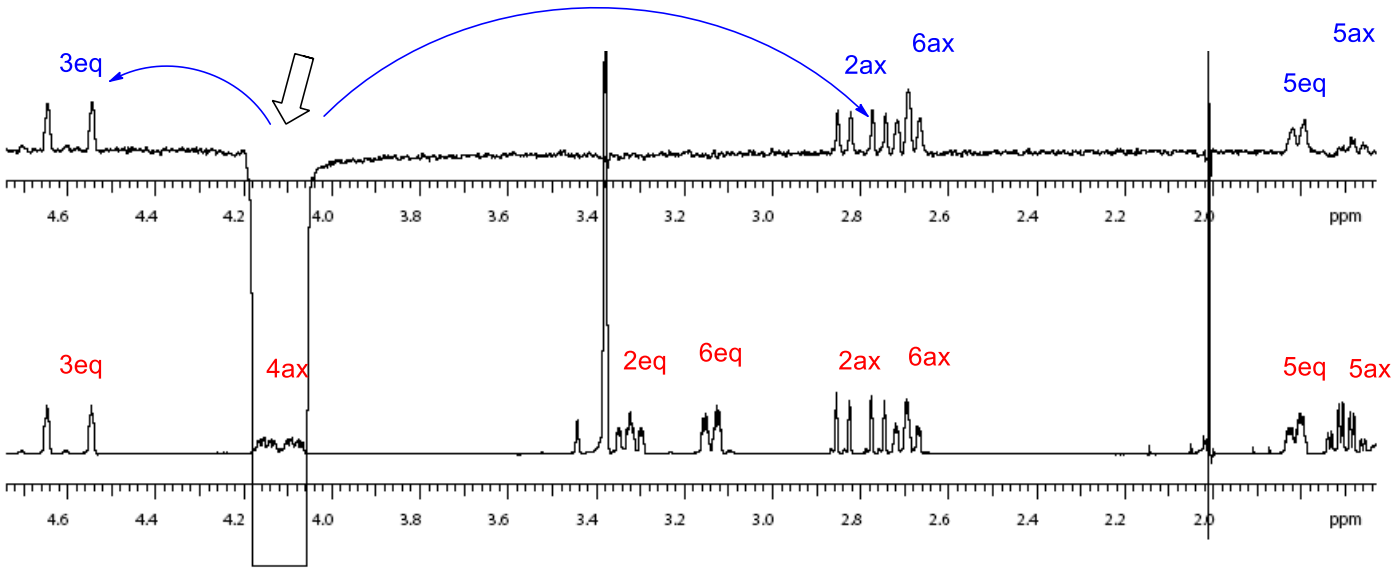




Relative Stereochemistry: 1D ^{1}H-^{1}H NOE Experiment

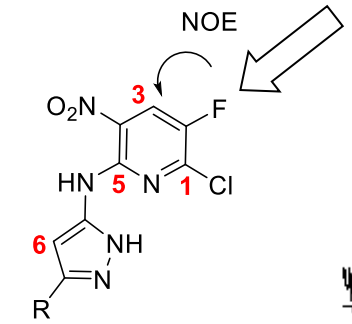
This problem can also be readily solved by ^{1}H-^{1}H J-coupling constants

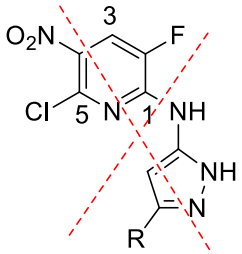


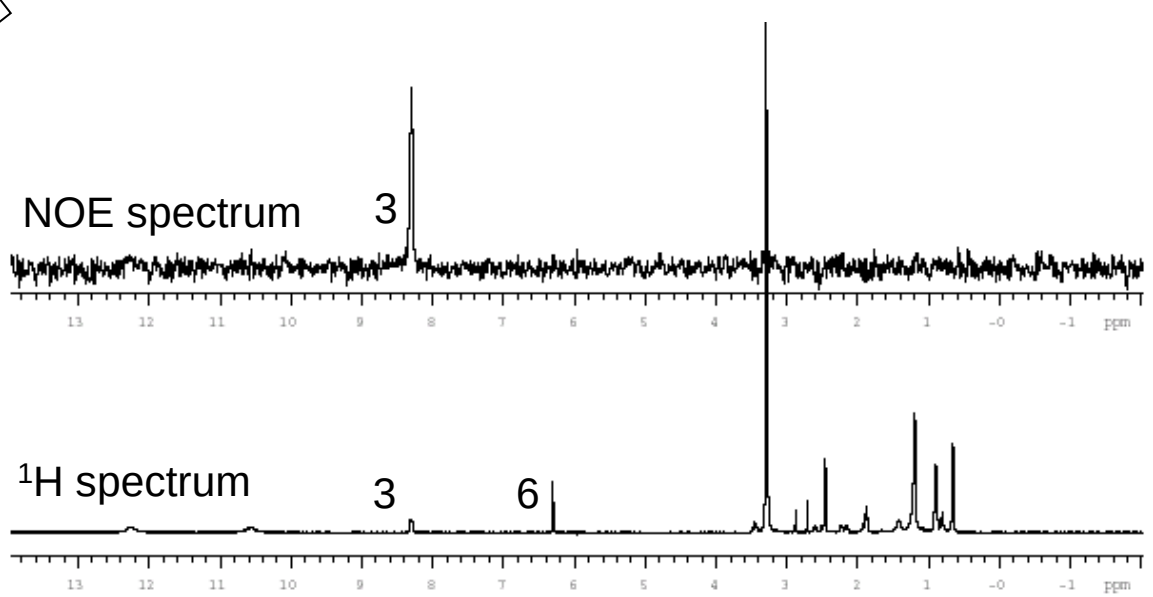


Regioisomer:
^{1}H-^{19}F NOE Experiment

NOE seen between ^{19}F and proton at position 3, but not to the pyrazole proton, suggesting the 5-position reaction, not 1-position.

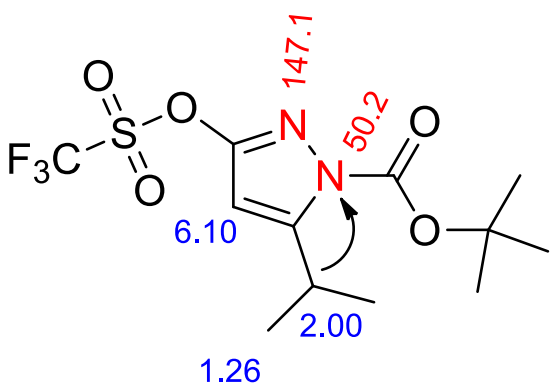


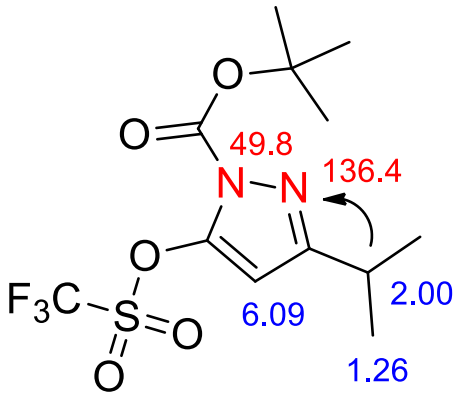




Regioisomer:
^{15}N Chemical Shifts

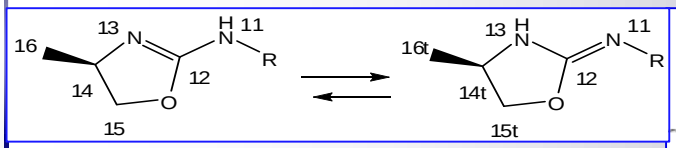
Based on the ^{15}N chemical Shifts and the connectivity from ^{1}H-^{15}N HMBC spectrum

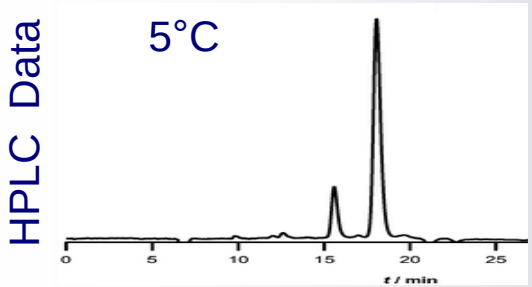


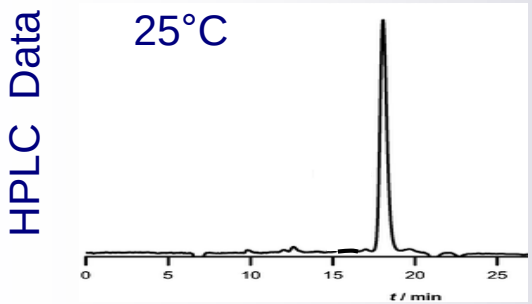


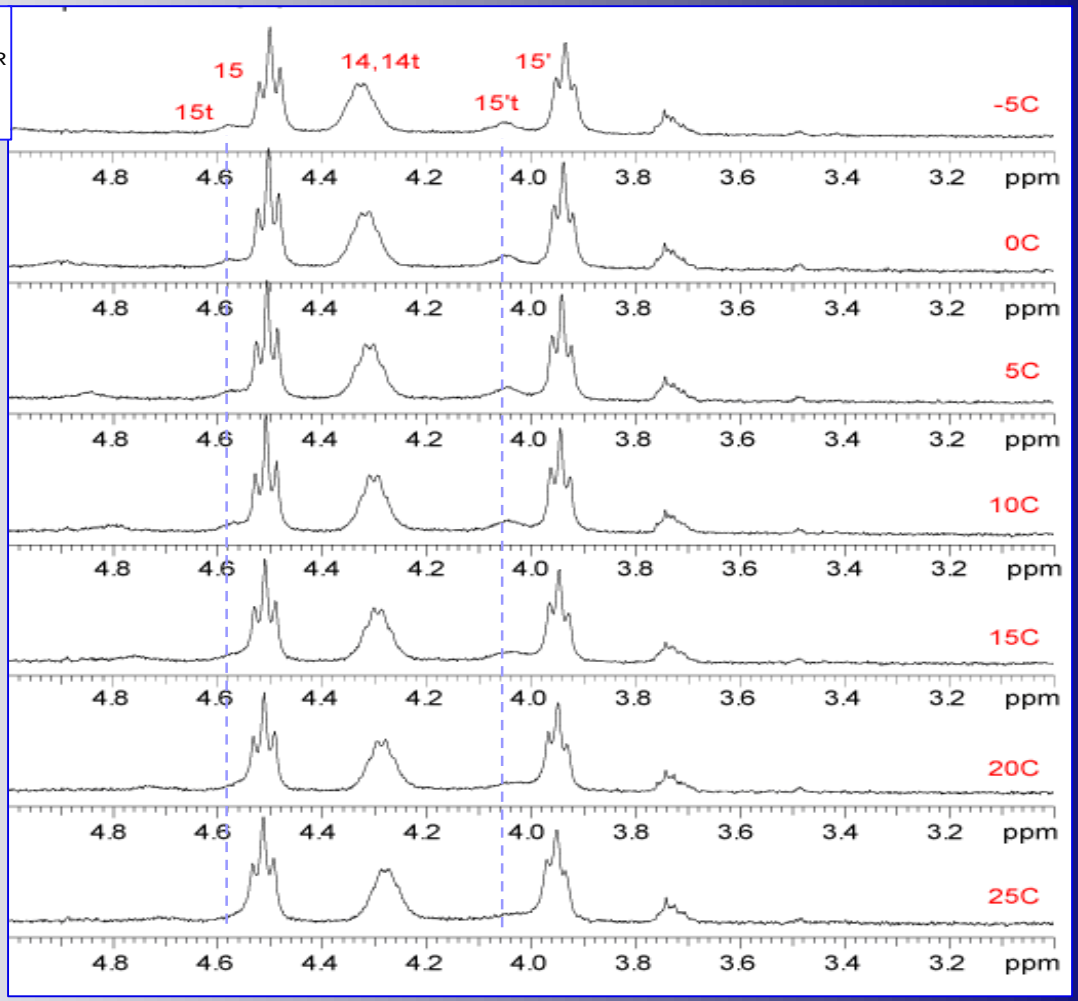
Variable Temperature Experiments: Tautomer Identification

Solution NMR in Organic Chemistry
Research Examples





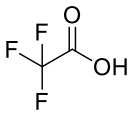




qNMR: Determination of %TFA by an Internal Standard

Solution NMR in Organic Chemistry
Research Examples

$$Cx = \left[\frac{3.47\text{mg}}{1\text{ mL}} \times \frac{1\text{mM}}{276}\right]\left[\frac{3}{3}\right]\left[\frac{121}{100}\right]$$

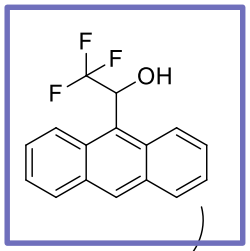


MW of TFA: 114
MW of the compound: 432

TFA measured: 0.01526 nM x 114 mg/mM = 1.734 mg

TFA %: 1.734 mg / 4.8 mg x100 = 36%

internal standard
MW: 276 in the tube
3.47 mg / 1 mL



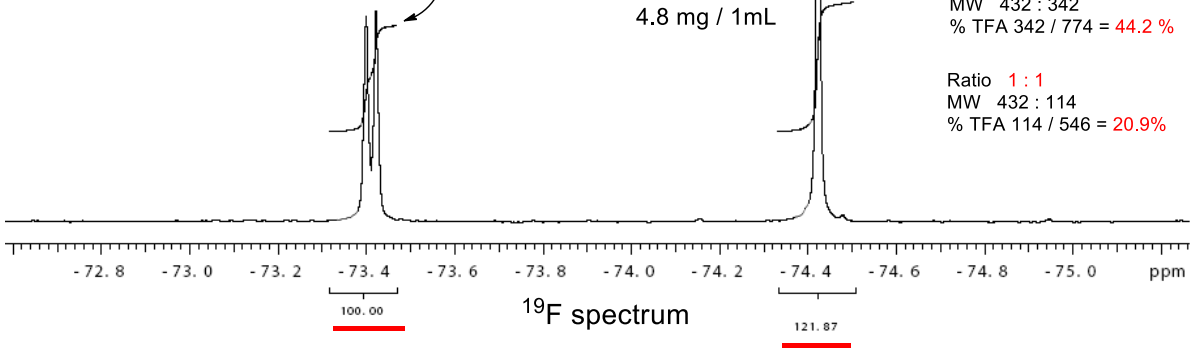
Theoritical Calculation:

Ratio 1 : 2
MW 432 : 228
% TFA 228 / 660 = 34.5%

weighted
compound/TFA
in the tube
4.8 mg / 1mL

Ratio 1 : 3
MW 432 : 342
% TFA 342 / 774 = 44.2 %

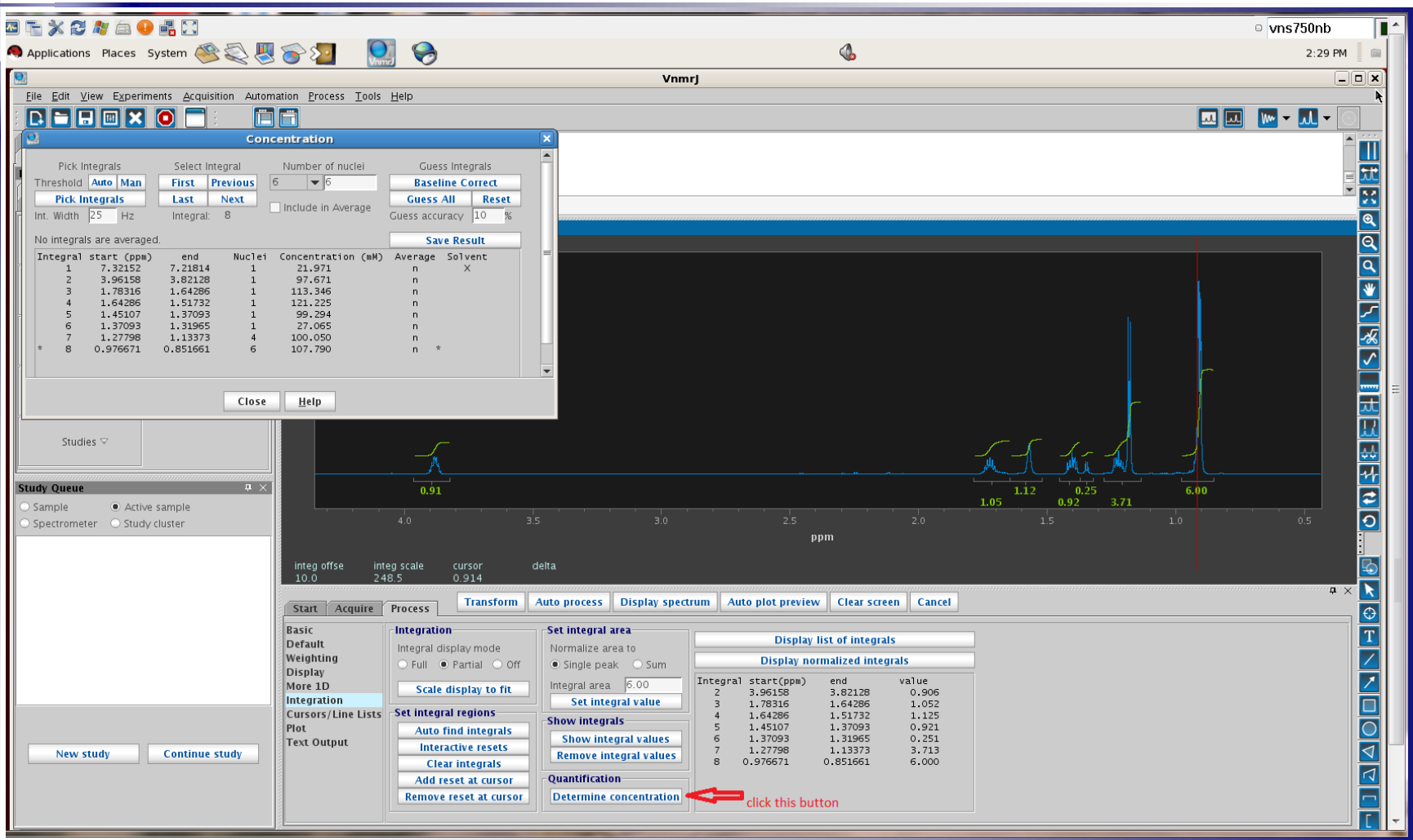
Ratio 1 : 1
MW 432 : 114
% TFA 114 / 546 = 20.9%



^{19}F spectrum

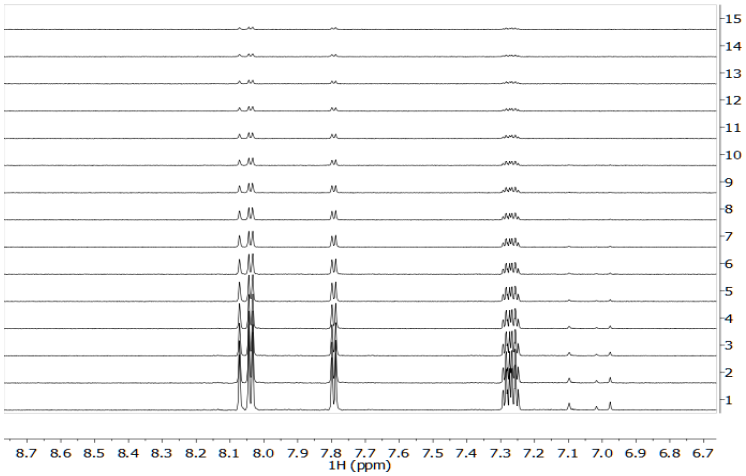
qNMR: Determining [sample] using NMR software

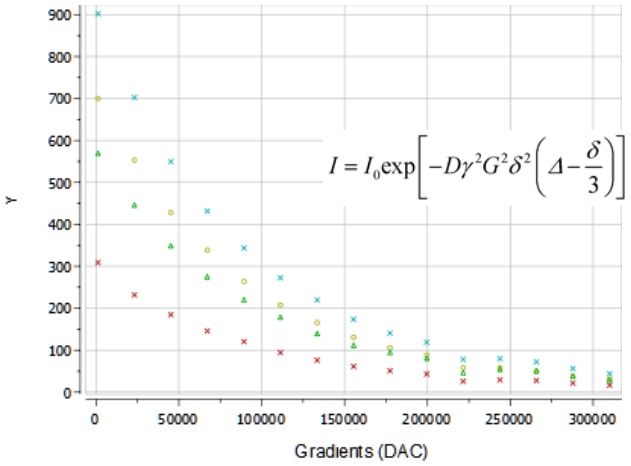
Solution NMR in Organic Chemistry
Research Examples

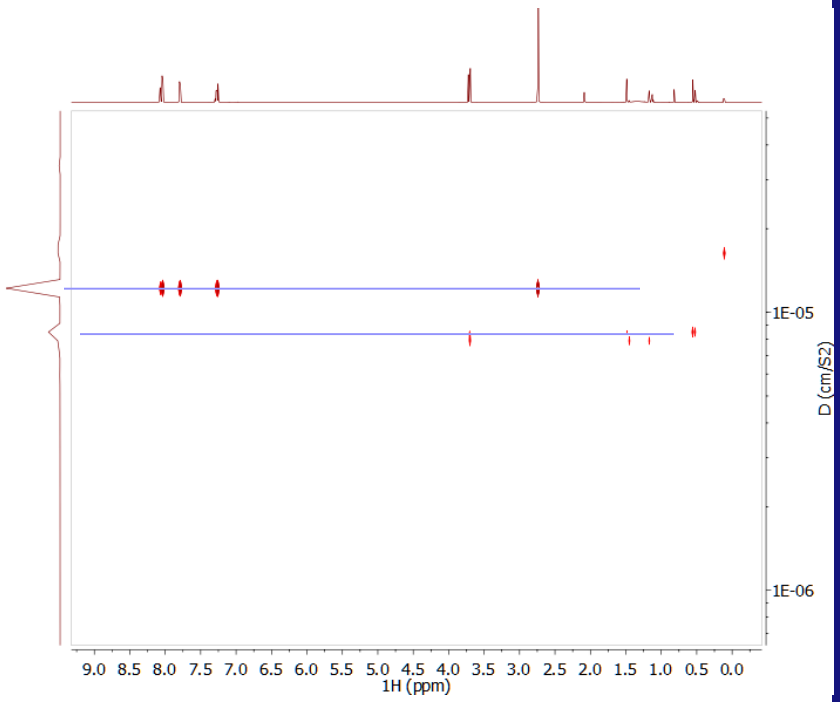


DOSY: Determination of MW / Mixture

Solution NMR in Organic Chemistry
Research Examples







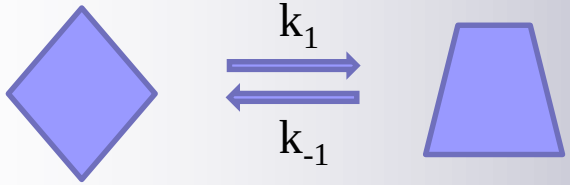
$D = kT/6\pi\eta r$

$MW = (4\pi r^3 \rho N)/3$

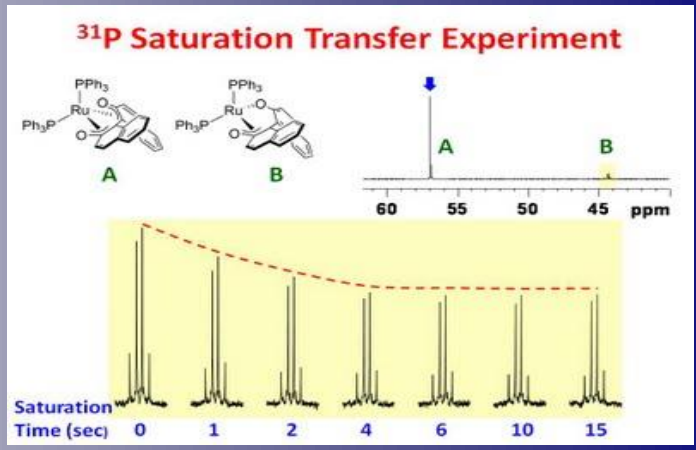
Chemical Exchange in NMR: Intra- and Inter-molecular process

Solution NMR in Organic Chemistry
Research Examples

Intra-

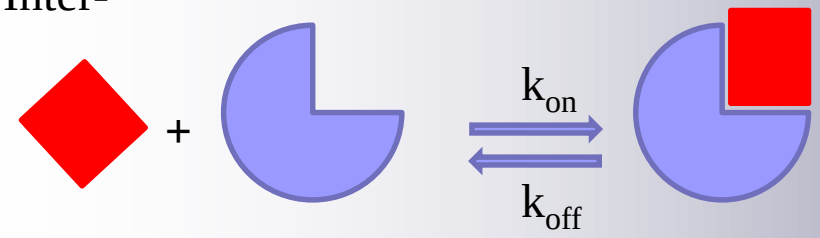


$\mathbf{K_{eq}}$ determined by LW and $\Delta\delta$

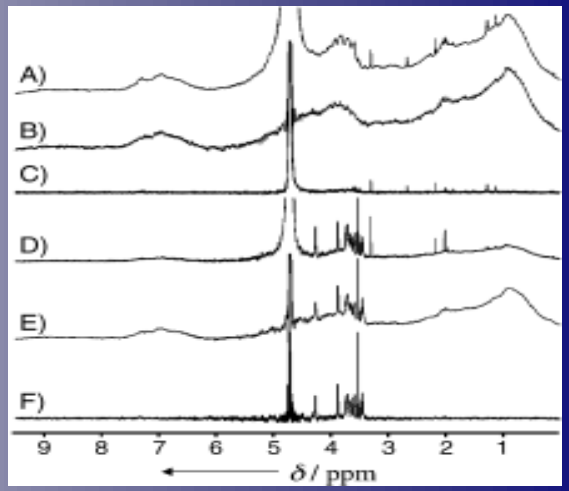


U. Ottawa NMR Facility

Inter-

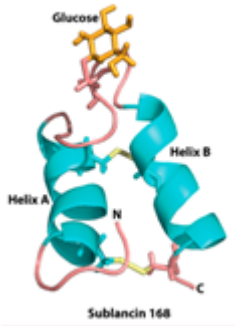


$\mathbf{K_{assoc}} = k_{on}/k_{off}$



STD Experiments
Meyer: 2003

Collaborations & Publications



Select Publications:

- Enzyme-mimetic, self-catalyzed polymerization of polypeptide helices. Nature Comm 2019 (**Cheng group**)
- Small on channels increase host defenses in cystic fibrosis airway epithelia. Nature 2019 (**Burke group**)
- Lithium-Olefin Pi Complexes and the Mechanism of Carbo-lithiation. Synthesis, Solution Behavior, and Crystal Structure of (2,2-Dimethylpent-4-en-1-yl. Organometallics, 2019 (**Girolami group**)
- Cobalt-Mediated ^{13}C NMR signal Enhancement using Parahydrogen Induced Polarization. JACS 2018 (**Fout group**)
- A Metal-Free Electrocatalyst for Carbon Dioxide Reduction to Multi-Carbon Hydrocarbons and Oxygenates. Nature Comm 2016 (**Kenis group**)
- The interplay of Al and Mg speciation in advanced Mg battery electrolytes. JACS, 2015 **(Gewirth group)**
- Control of protein orientation on gold nanoparticles. JPC, 2015 **(Murphy group)**
- Structure, bioactivity, and resistance mechanism of streptomonomicin, an unusual lasso peptide from an understudied halophilic actnomycete. Chem Biol 2015 **(Mitchell group)**
- Alkyne Mechanochemistry: Putative Activation by Transoidal Bending. RSC ChemComm. 2014 **(Moore group)**
- NMR structure of the S-linked glycopeptide sublancin 168. ACS Chem Biol. 2014 **(van der Donk group)**
- New Reactions of Terminal Hydrides on a Diiron Dithiolate. JACS 2014 **(Rauchfuss group)**

Thank you

Please visit us at http://scs.illinois.edu/nmr/
Questions Always Welcome

HuiHui, Xixi and Lu