UCLM
UNIVERSIDAD DE CASTILLA-LA MANCHA

Espectroscopia de Resonancia Magnética Nuclear

M. Victoria Gómez Almagro

17th July, 2019

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INTRODUCTION

NMR INSTRUMENTATION

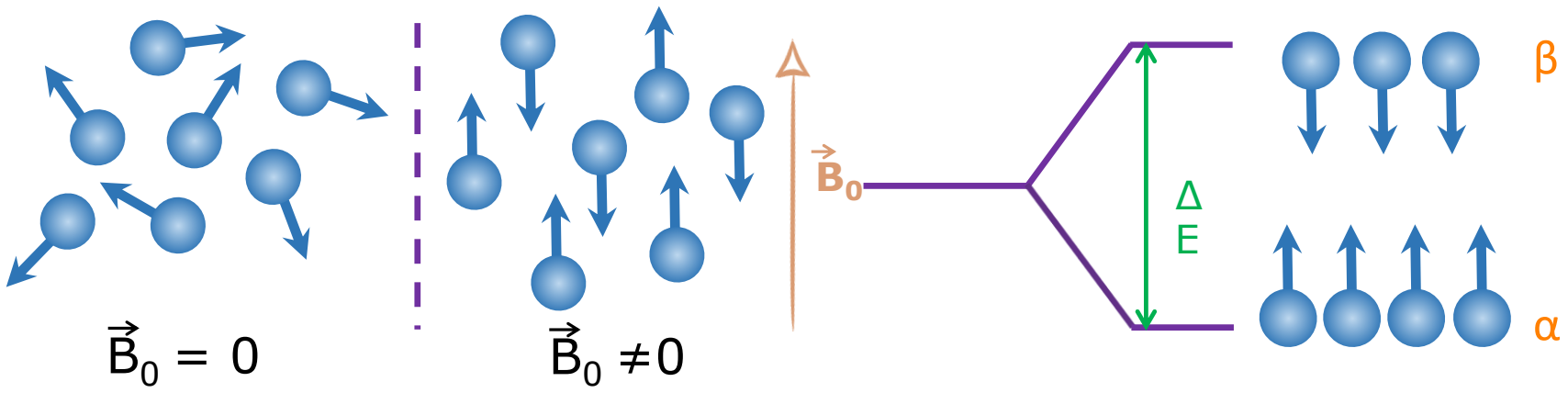
STEPS IN AN NMR ANALYSIS

STRUCTURAL IDENTIFICATION AND OTHER NMR APPLICATIONS

APPLICATIONS

- Structure identification.
- Reaction monitoring and kinetic investigations
- Reaction mechanism. Detection of intermediates
- Metabolomics
- Molecular size and aggregates: Diffusion NMR
- Monitorization of Dynamic process

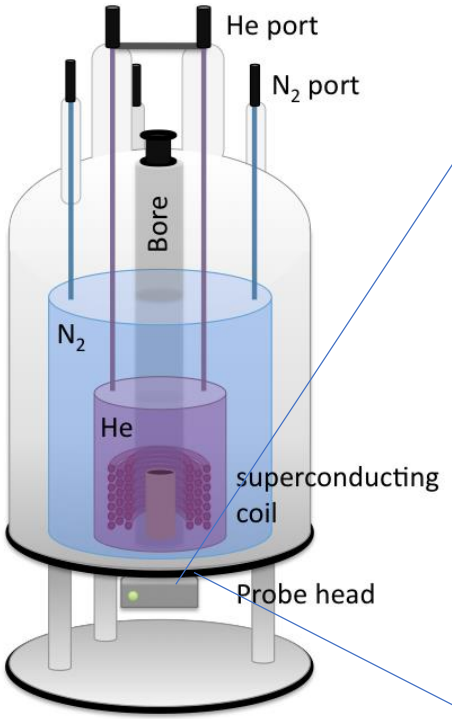
INTRODUCTION

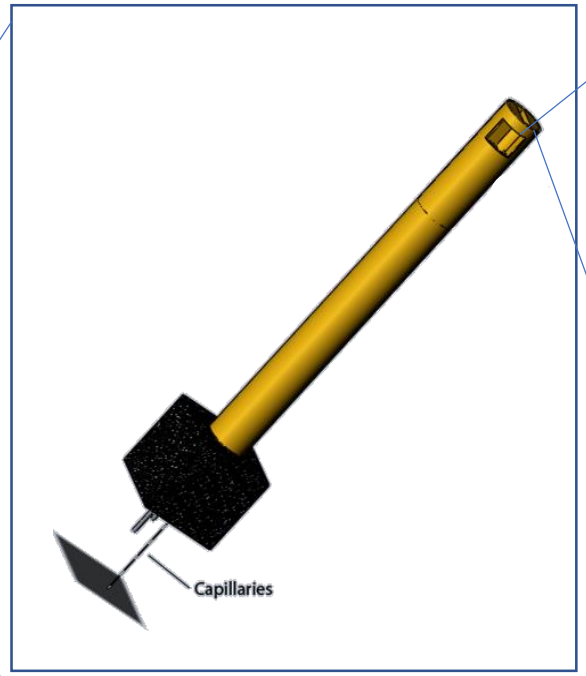


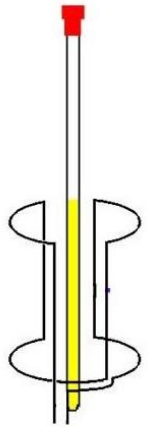
Powerful technique

Non destructive

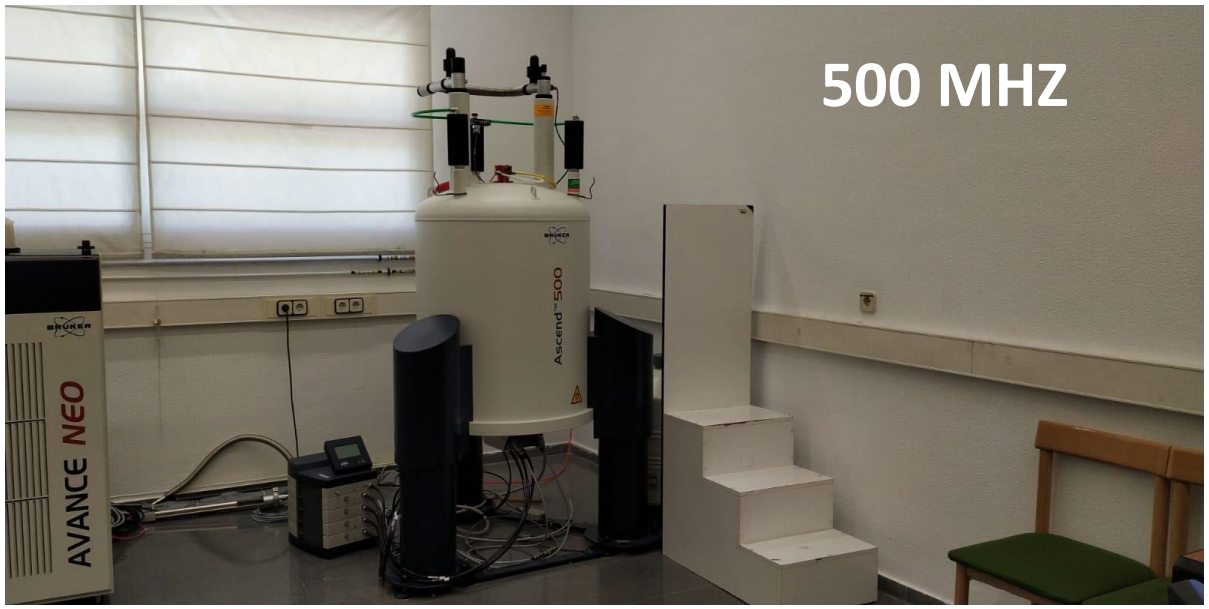
Low sensitivity







OUR EQUIPMENT



Triple resonance probe
TXI (500 MHz)

Higher ^{1}H sensitivity
More suitable for ^{15}N

iProbe
(400 y 500 MHz)

Universal.
Suitable for all nuclide

www.bruker.com

Different probes → Different aplications

Every NMR analysis consists of:

NMR sample preparation

Liquid samples: 500 µL
>1 mg

(Probes for solid and semisolids samples)

Acquisition of NMR spectra

1D MULTINUCLEAR

2D MULTINUCLEAR

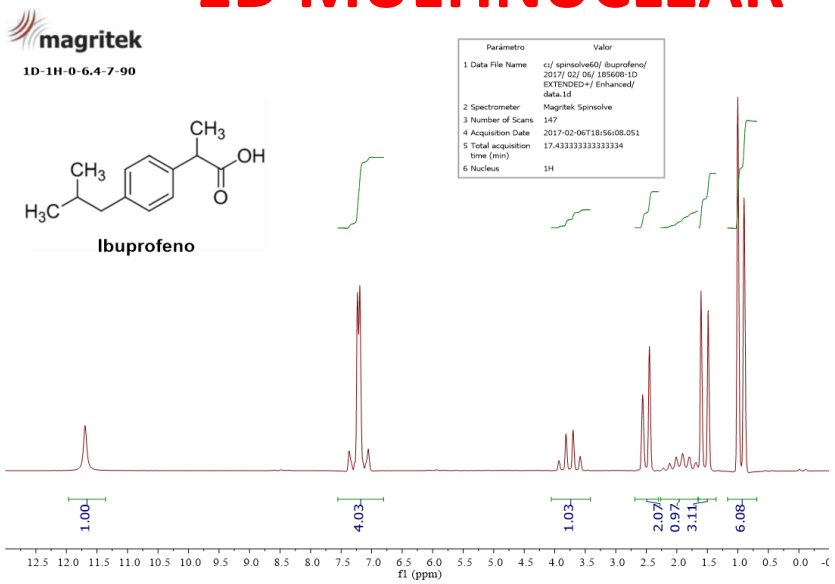
- $^{1}H,^{1}H$-COSY
- $^{1}H,^{1}H$-NOESY
- $^{1}H,^{13}C$-HSQC
- $^{1}H,^{13}C$-HMQC
- $^{1}H,^{13}C$-HMBC
- $^{19}F,^{13}C$-HSQC
- $^{19}F^{13}C$-HMBC

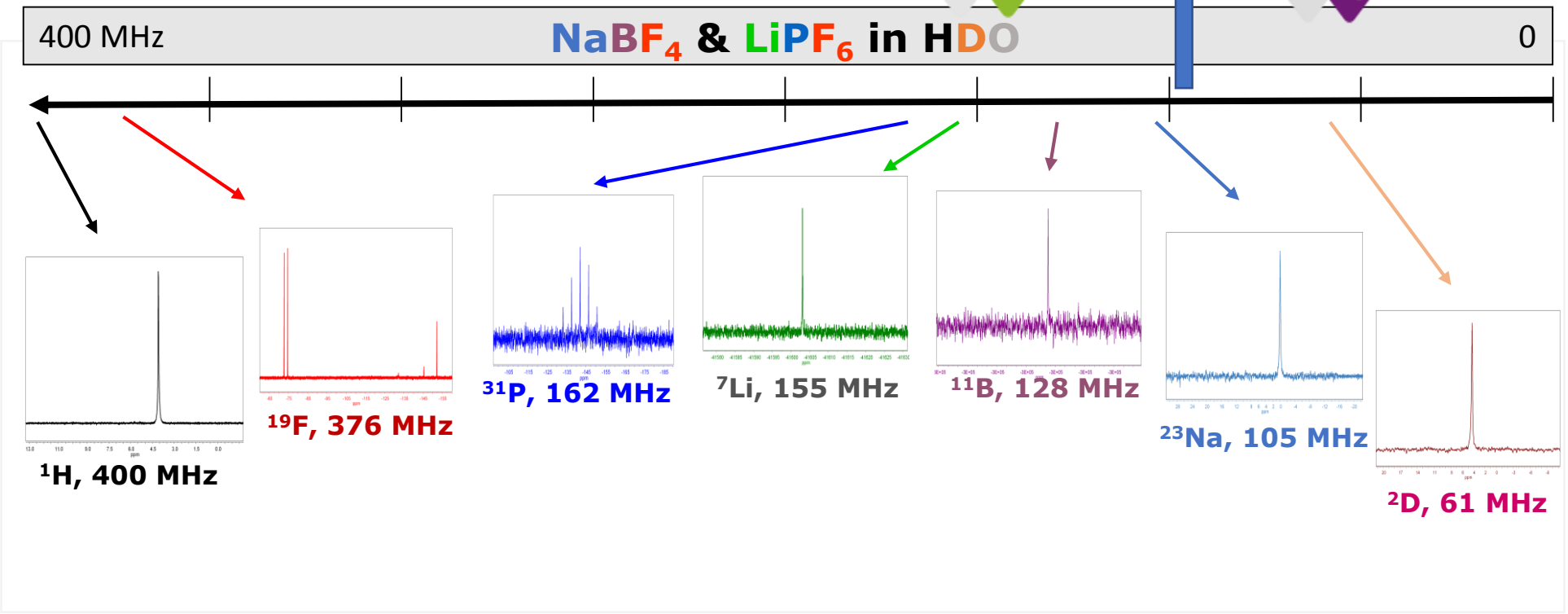
NMR assignment

Structure determination

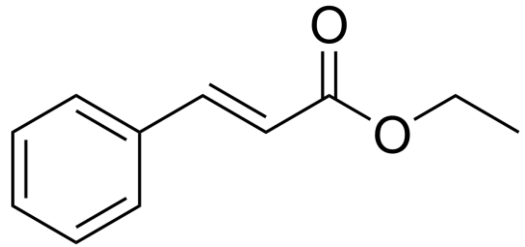
1D MULTINUCLEAR

Looking at all frequencies



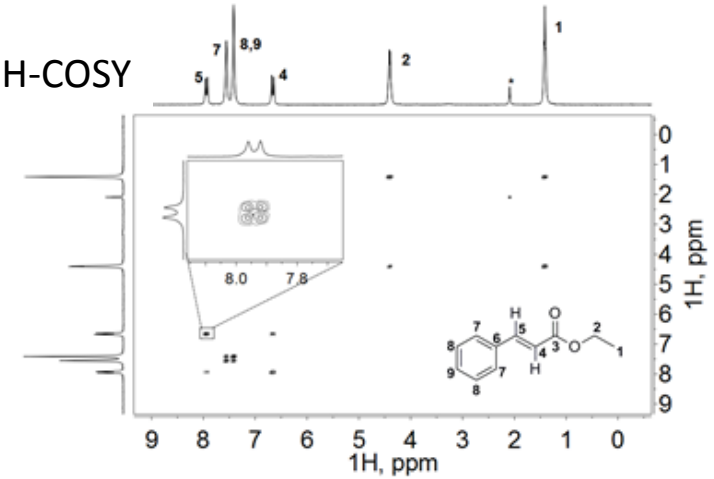


2D MULTINUCLEAR

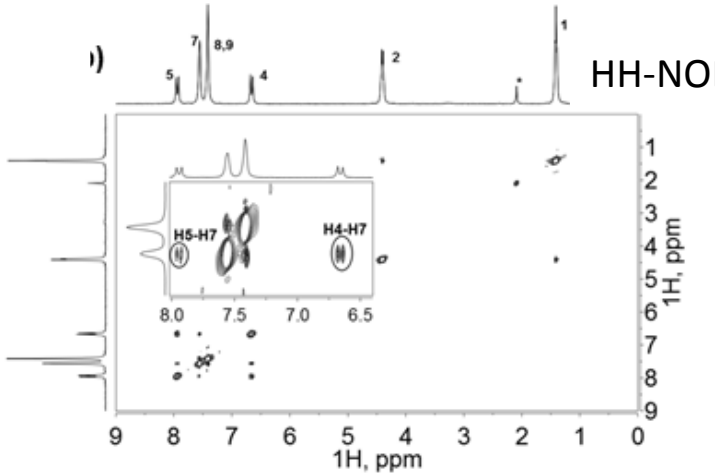


ethylcinnamate (~ flavor in 1 pepernoot …)

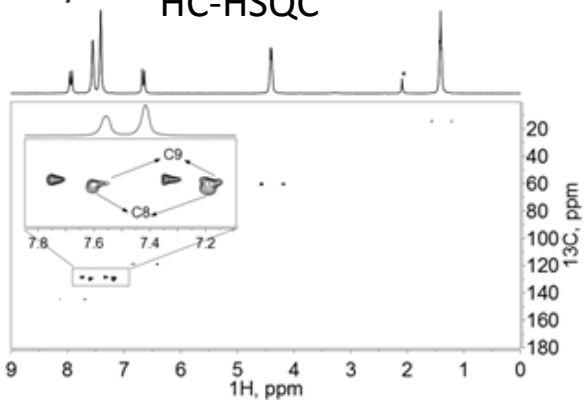
HH-COSY



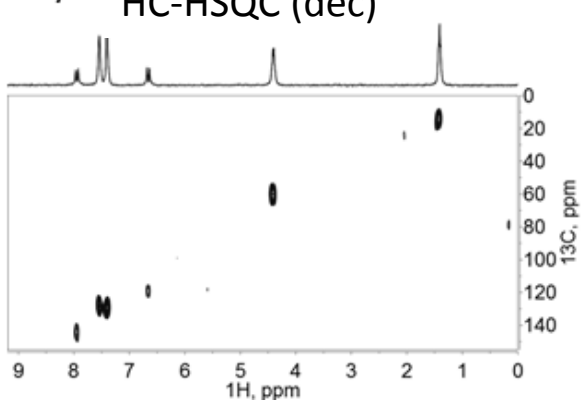
HH-NOESY



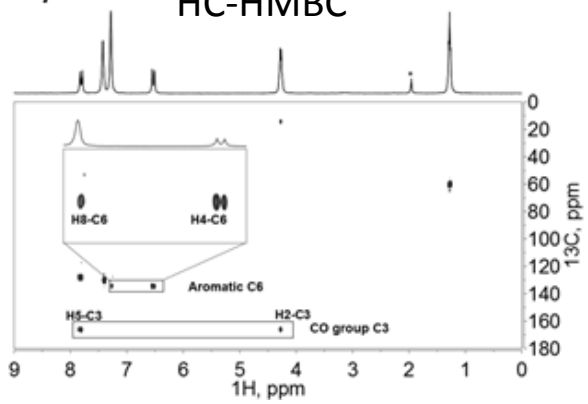
c) HC-HSQC



d) HC-HSQC (dec)



e) HC-HMBC



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(Probes for solid and semisolids samples)

Acquisition of NMR spectra → 1D MULTINUCLEAR

NMR assignment → PEAK IDENTIFICATION

2D MULTINUCLEAR

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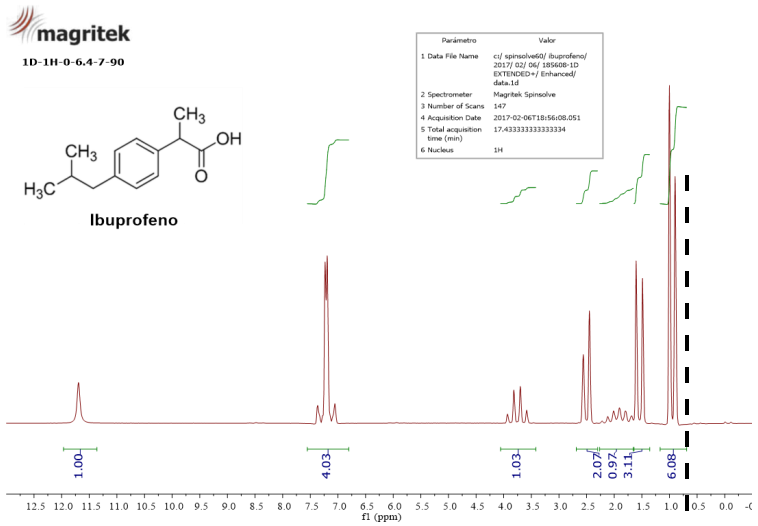
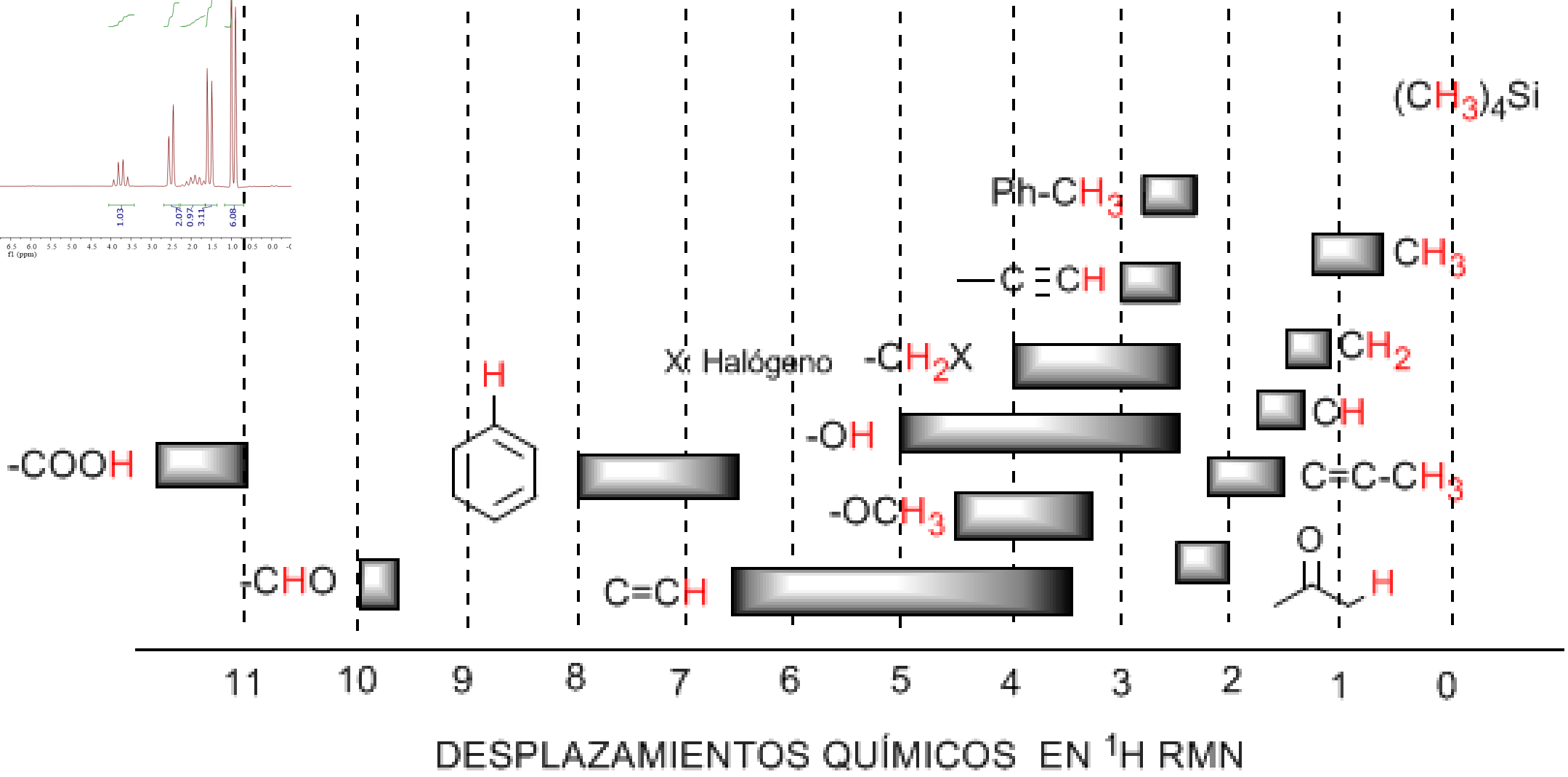
Structure determination

PEAK IDENTIFICATION





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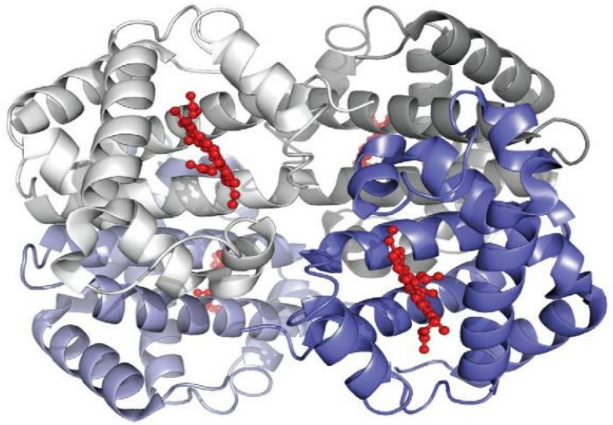
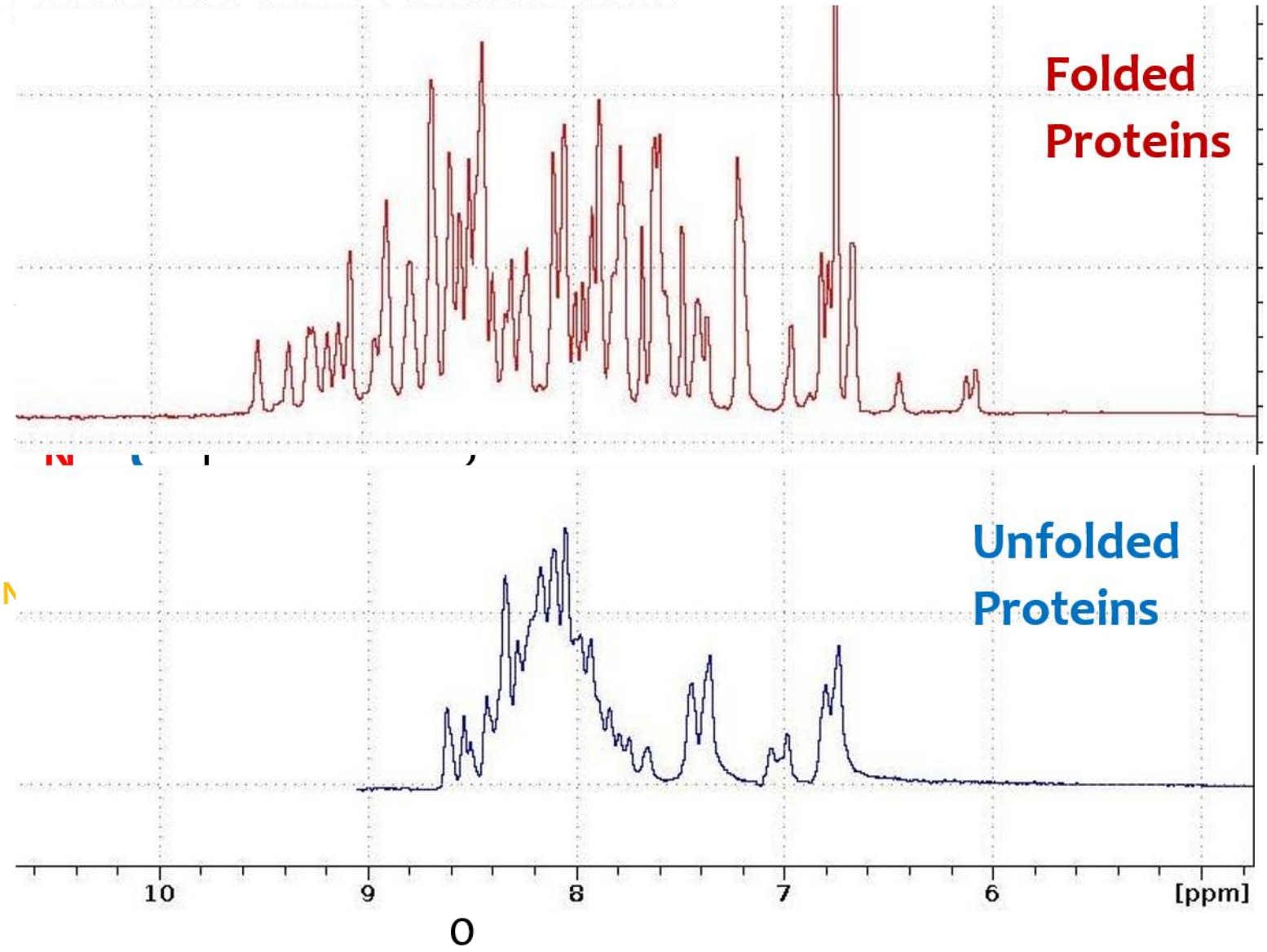
NMR assignment → PEAK IDENTIFICATION

Structure determination →



STRUCTURE IDENTIFICATION. i.e. PROTEINS



APPLICATIONS

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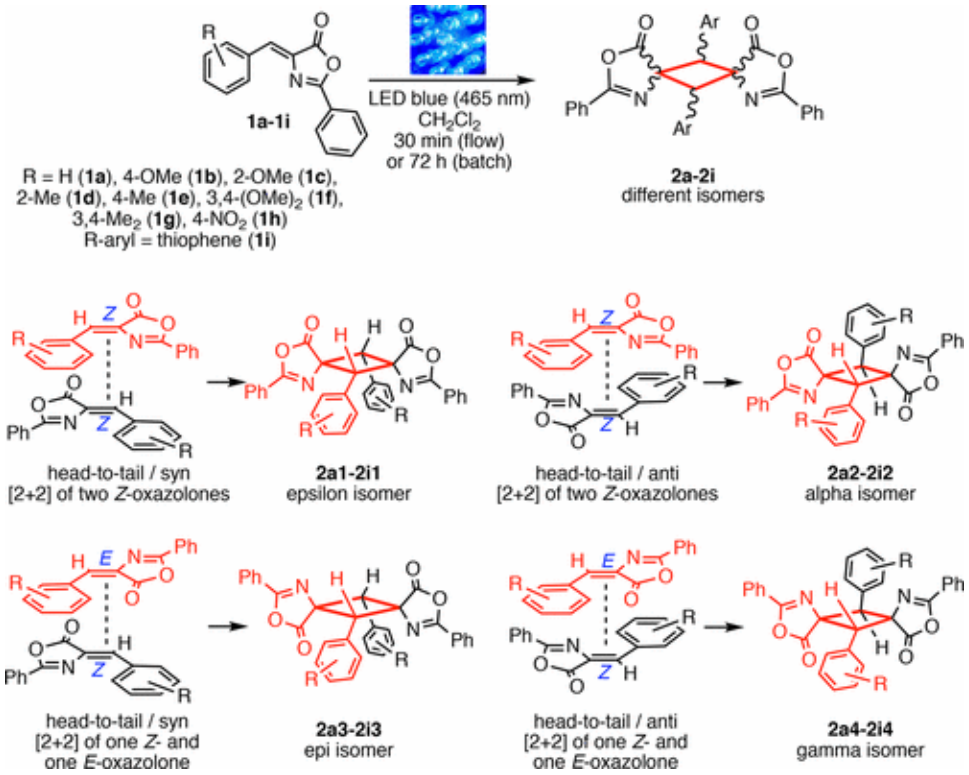
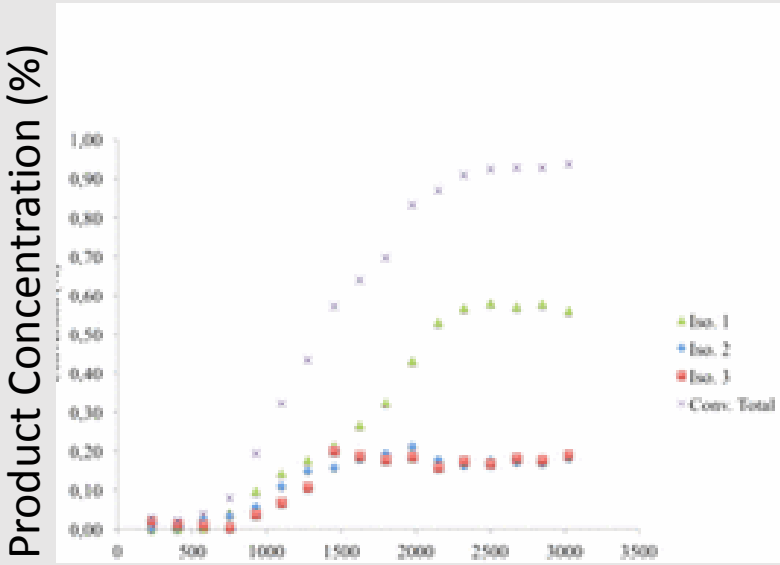
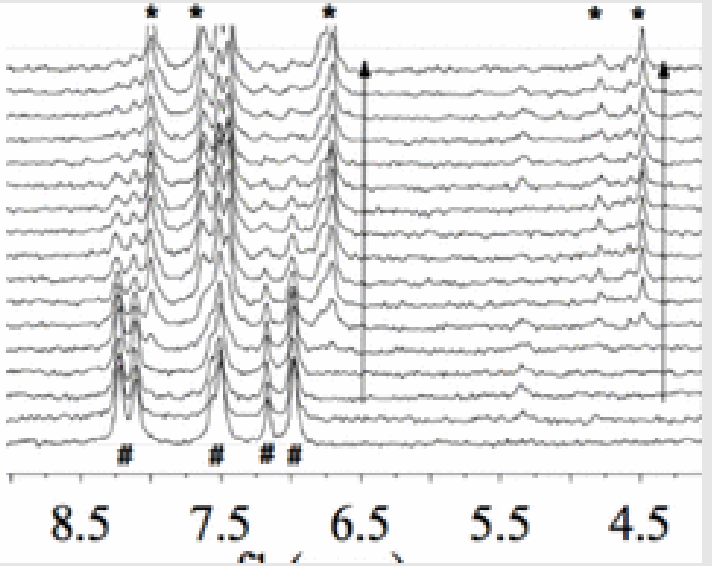
REACTION MONITORING. KINETIC INVESTIGATIONS







Garcia-Montero et al., *ACS Sustainable Chem. Eng*. **2017**, *5*, 9, 8370-8381.

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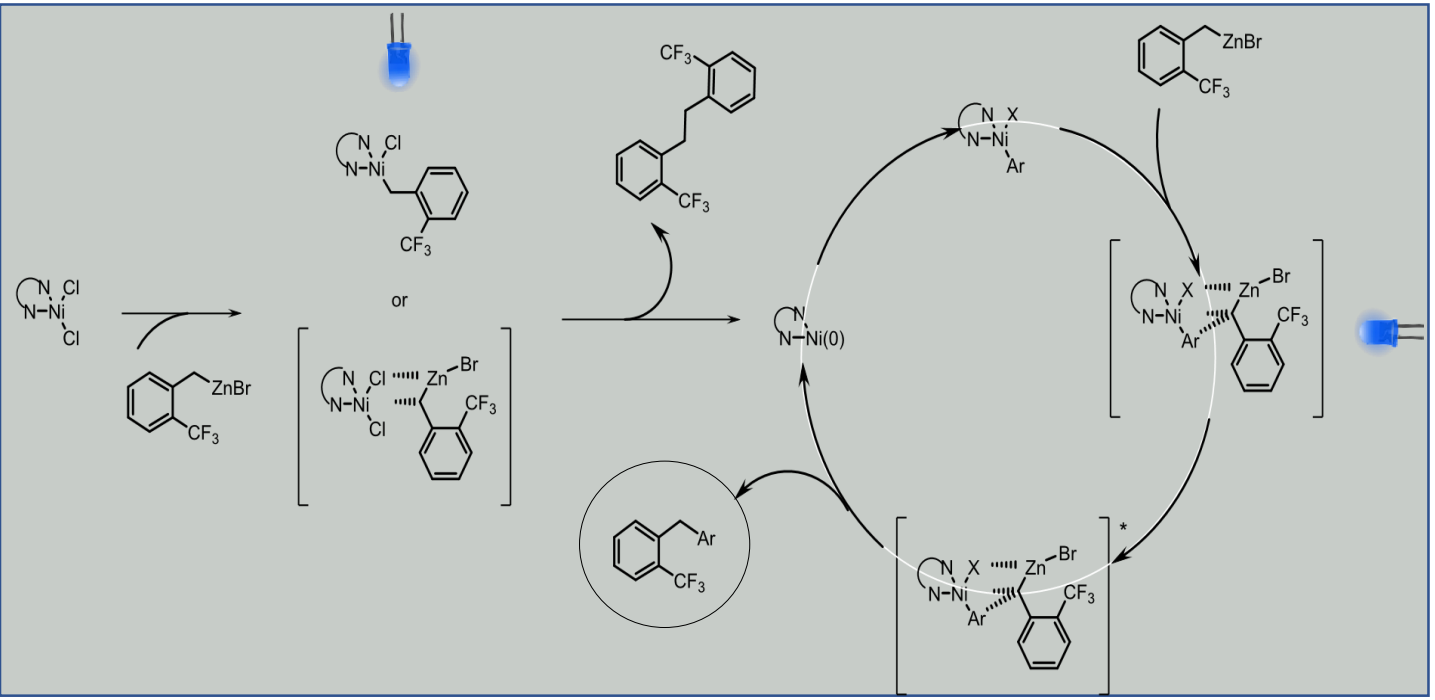
MECHANISM ELUCIDATION. DETECTION OF INTERMEDIATES

Visible-Light-Induced Nickel-Catalyzed Negishi Cross-Couplings by Exogenous-Photosensitizer-Free Photocatalysis



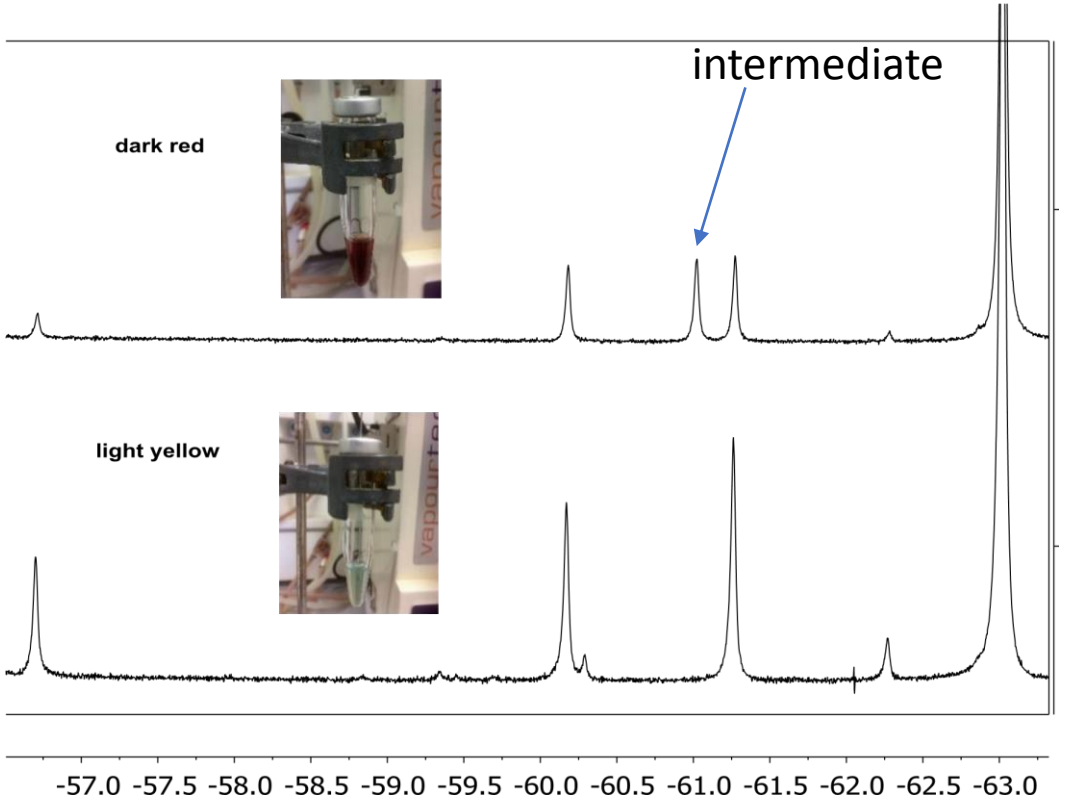


Figure S5: Top: ^{19}F NMR spectrum after a quick addition of the zincate derivative over the Nickel complex. The solution turned a dark red color. Bottom: ^{19}F NMR spectrum of the reaction mixture within time and after light irradiation. The peak at -61 ppm has disappeared and the reaction media lost its dark red color.

Abdiaj et a. *Angew. Chem. Int. Ed*. **2018**, *57*, 8473

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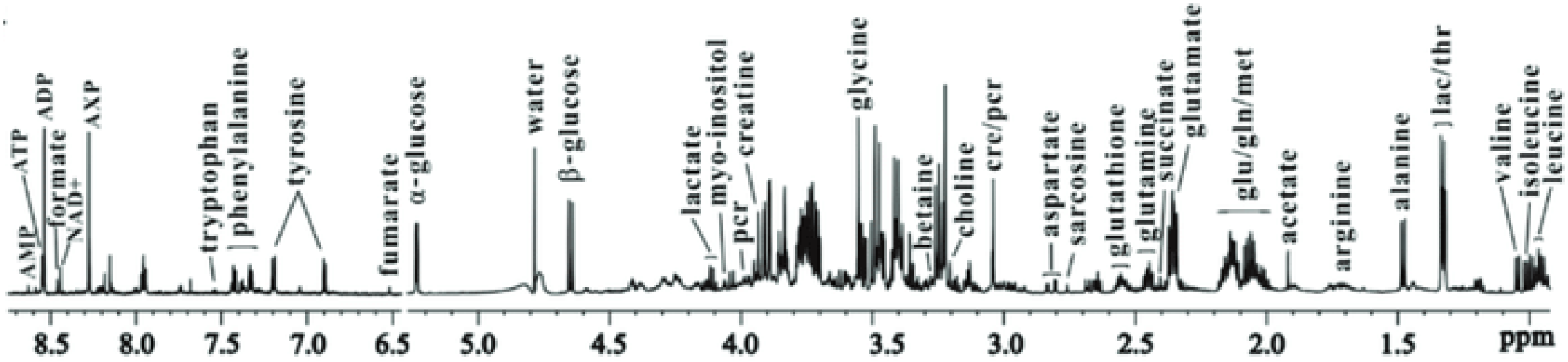
METABOLOMICS

BLOOD PLASMA
URINE OR
CELL EXTRACTS



1H NMR (ppm) of cell extracts

Zhang et al., *Molecules*, **2018,** *23(4)*, 807

METABOLOMIC APPROACH

POPULATION
(I.E. CONTROL /DISEASE)

→

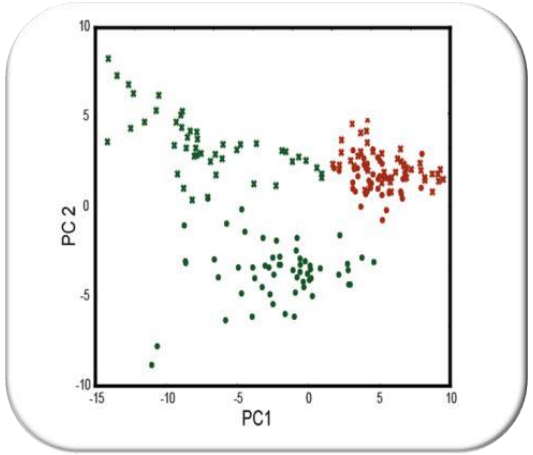
COLLECTION OF SAMPLES
(preparation, storage)

→

CHEMICAL ANALYSES (Ii.e. 1H NMR)

↓

DATA PROCESSSING (x,y matrix)



←

metabolite		d (ppm)
ethanol		1,218
alanine		1,525
ethanol		3,690
alanine		3,842
b-glucose		4,703
a-glucose		5,291

←

METABOLITES SIGNIFICANTLY DIFFERENT IN CONTROL / DISEASE SAMPLES

BIOMARKERS

-43 metabolites identified in human Blood Plasma by 750 MHz 1H and 1H-13C NMR spectroscopy:
Anal. Chem. **1995**, *67*, 793-811.

APLICATION OF METABOLOMICS

PHARMACEUTICAL DISCOVERY DISEASE

DIAGNOSIS AND DEVELOPMENT

ENVIRONMENTAL METABOLOMICS

PLANT METABOLOMICS

FOOD AND NUTRITION SCIENCE

ECOMETABOLOMICS

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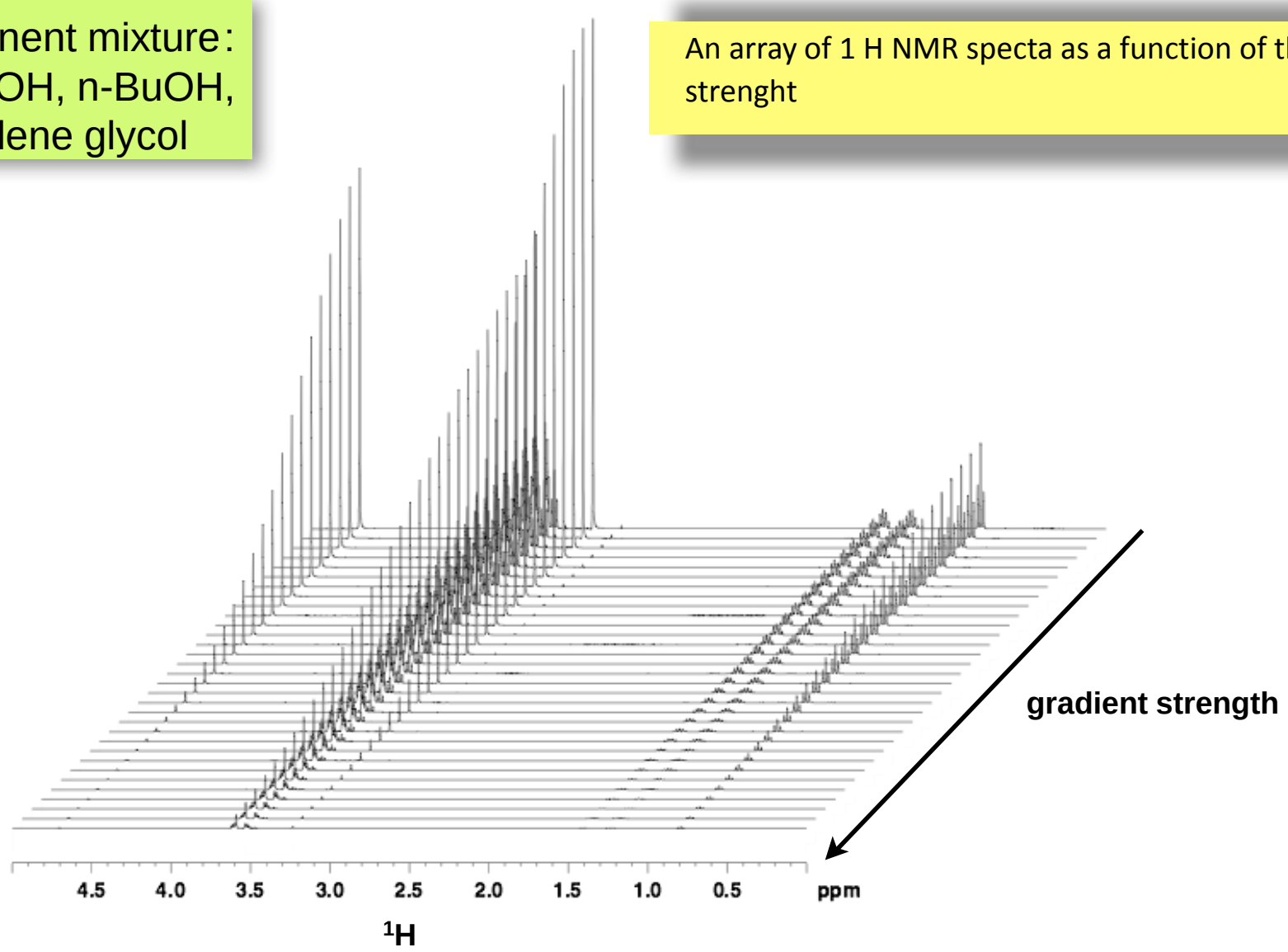
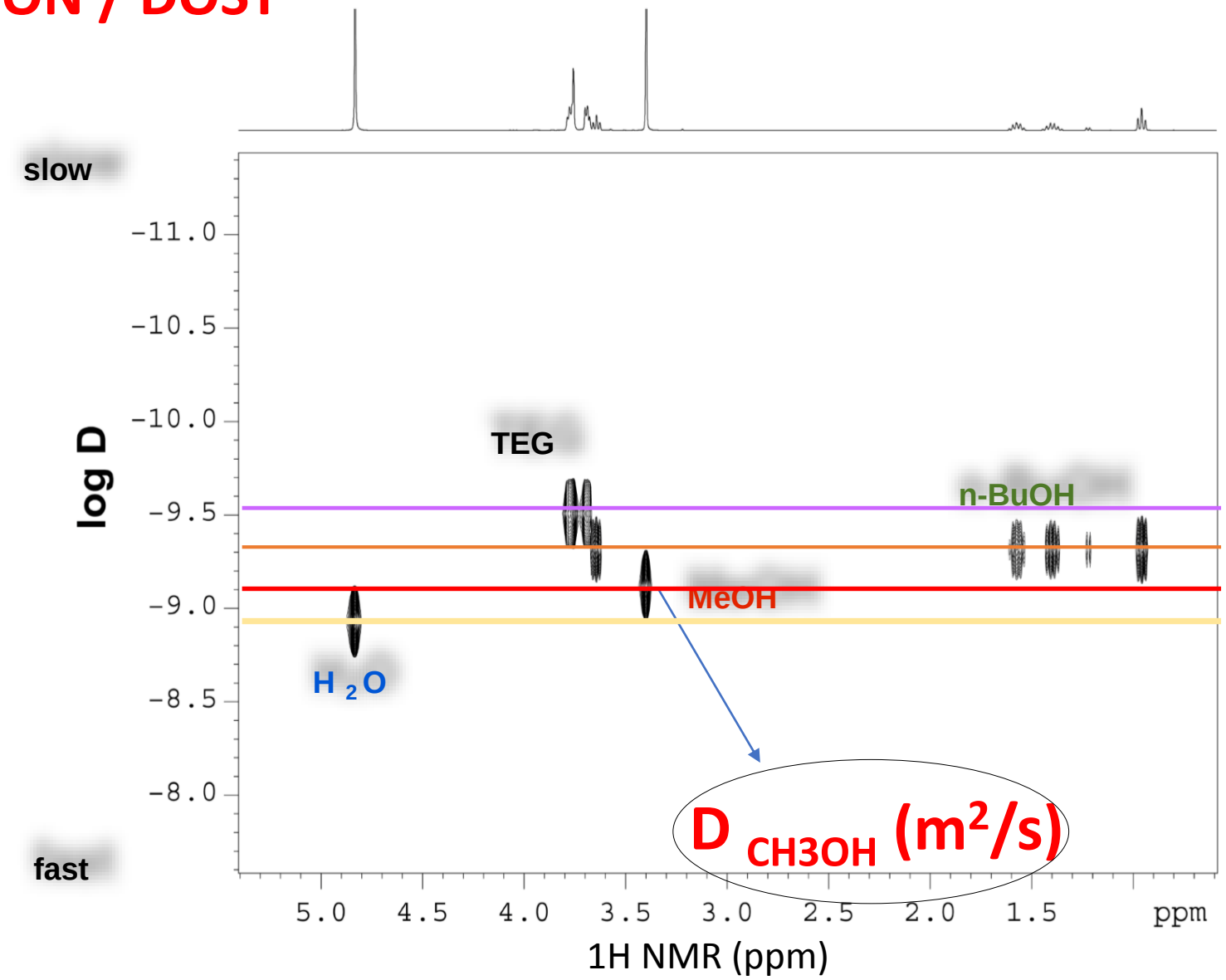
DIFFUSION / DOSY

4 component mixture: H_2O, MeOH, n-BuOH, triethylene glycol

An array of 1 H NMR specta as a function of the gradient strenght



DIFFUSION / DOSY



Ratio in size: **TEG** > **n-BuOH** > **MeOH** > H2O

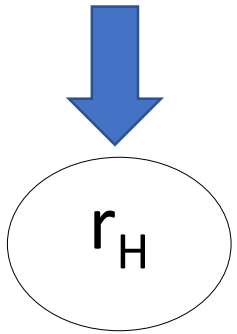
Quantitative diffusion studies

If the r_H of the standard is known the r_H of the sample can be determined

The ratio of the diffusion of a particular compound and the reference will be independent of the viscosity

$$\frac{D}{D_{ref}} = \frac{r_{Href}}{r_H}$$

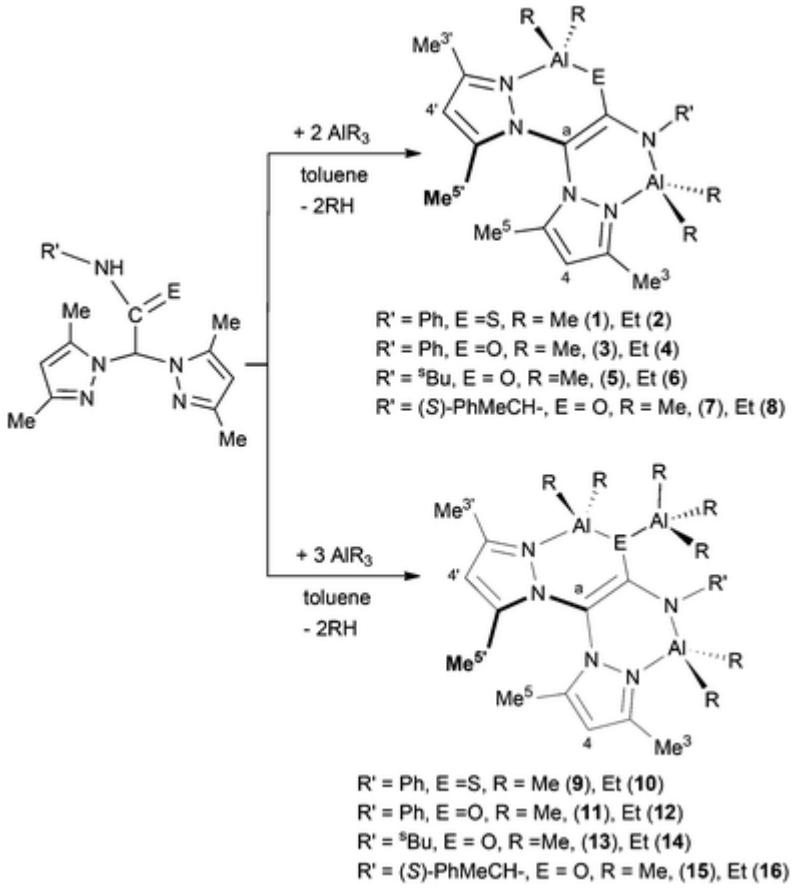
The use of a diffusion standard (D^{ref})

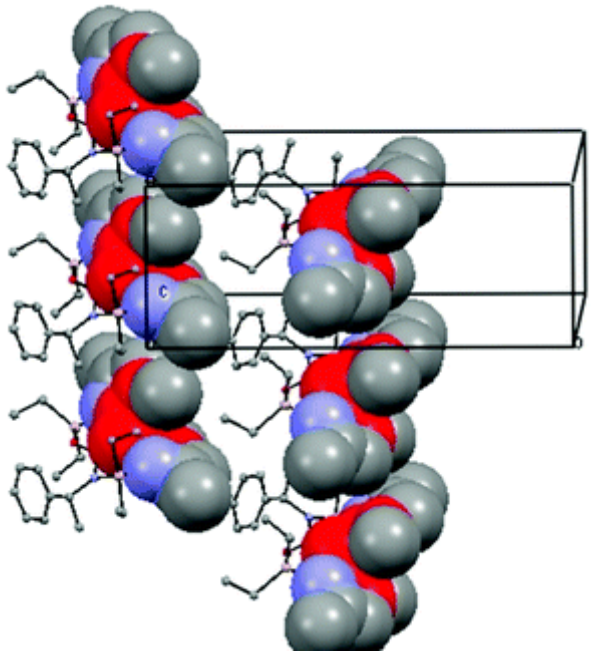


Magn. Reson. **2001**, *39*, s142-s148

Heteroscorpionate aluminium complexes as chiral building blocks to engineer helical architectures

Dalton Trans., **2013,** *42*, 14240-14252





C (mM)	D_t (10^{-10} m^2/s)	r_H	V	N
10	10.4	5.46	0.6	1
50	8.3	6.85	1.3	1.90
100	7.05	7.46	1.7	2.55
300	5.9	8.0	2.1	3.20
500	4.8	8.6	2.7	3.93

APPLICATIONS

- Structure identification.
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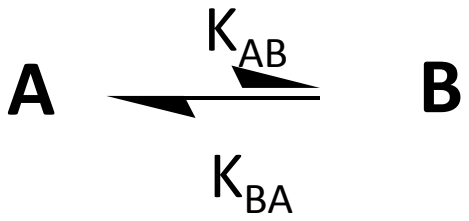
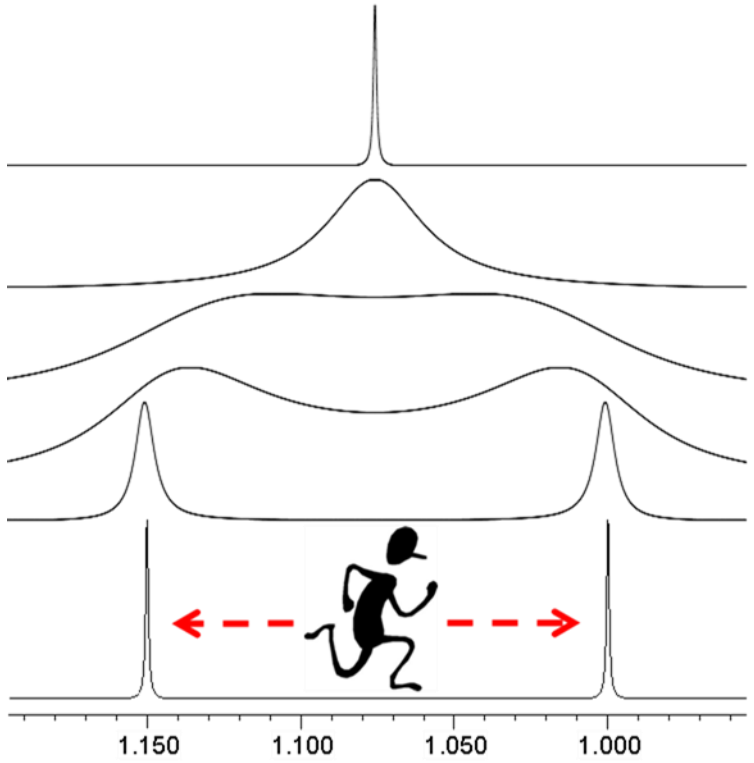
DYNAMIC PROCESSES /CHEMICAL EXCHANGE



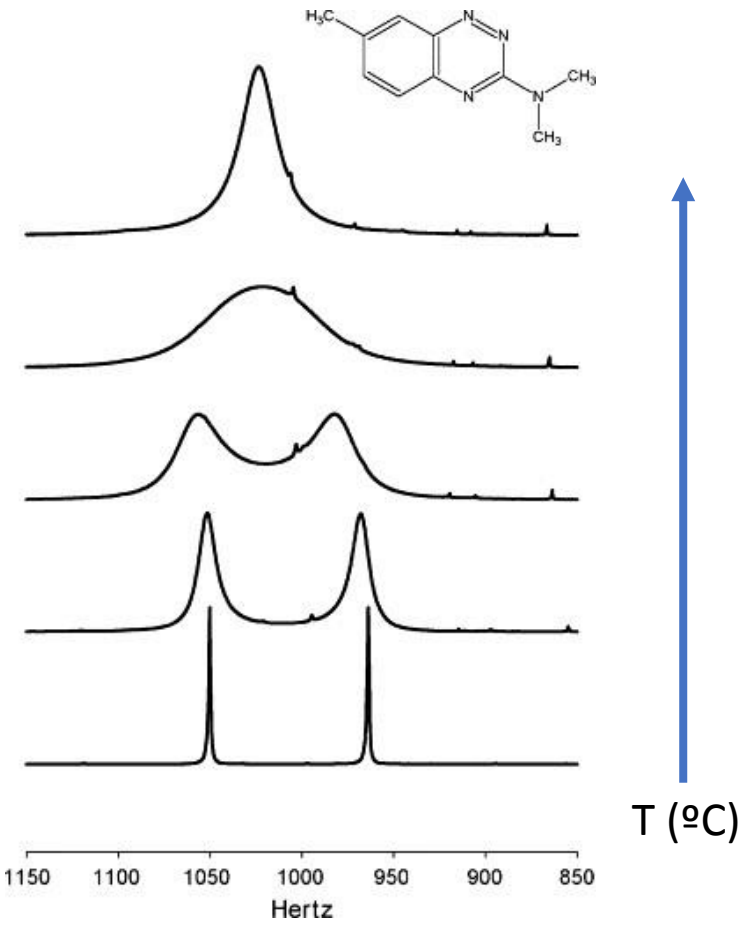


Fast exchange

intermediate

Slow exchange

Ej. Typical example:
Variable temperature measurements



Other examples: axial-equatorial Exchange
keto-enol tautomerism

Can. J. Chem. **1994**, *72*, 382

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ESPECTROSCOPIA DE RESONANCIA MAGNETICA NUCLEAR

M. Victoria Gomez Almagro

17th July, 2019