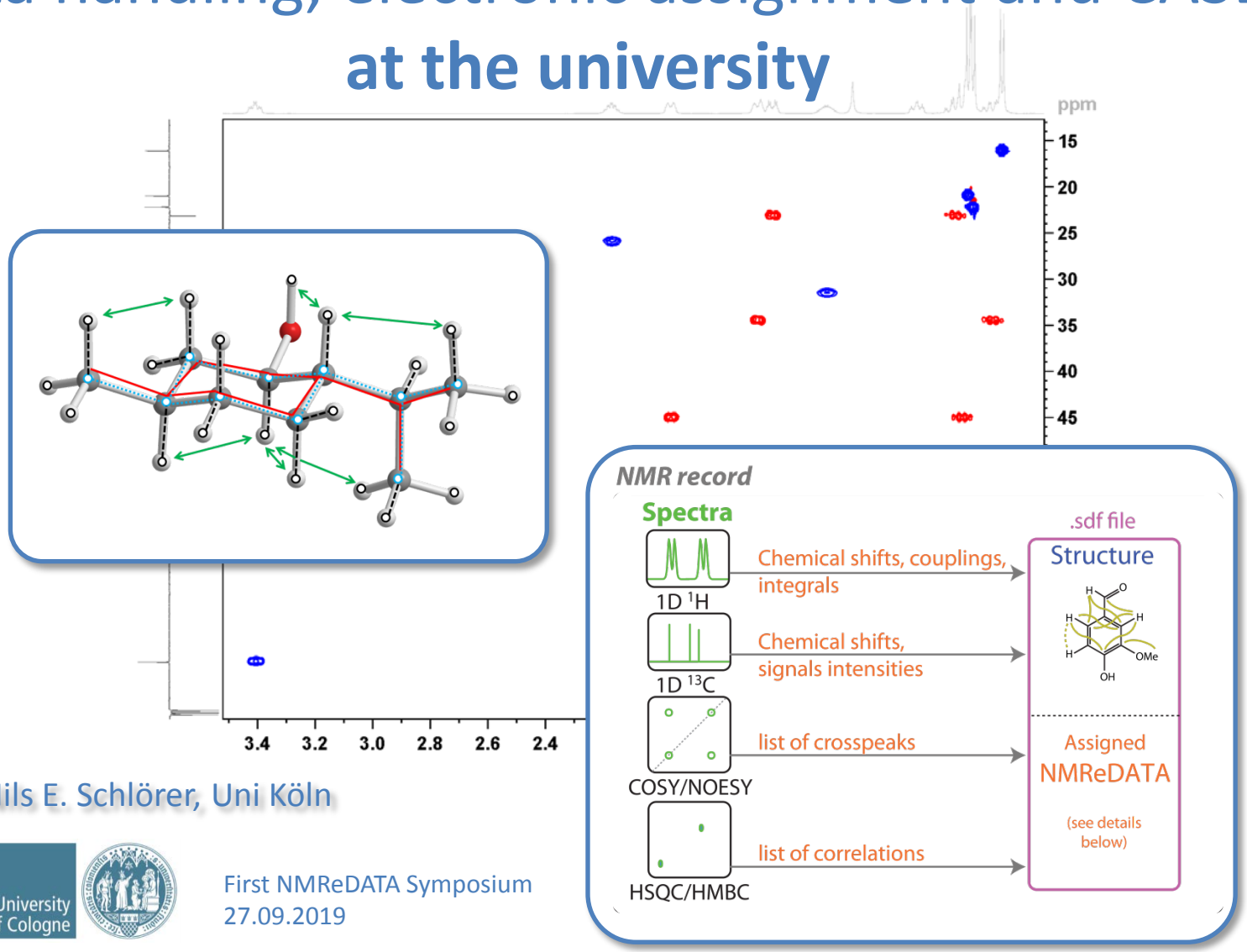
Teaching NMR

data handling, electronic assignment and CASE **at the university**



Nils E. Schlörer, Uni Köln

University of Cologne

First NMReDATA Symposium
27.09.2019

Content

(1) Current situation - where we are ...

(2) Teaching - examples, experiences & thoughts

(3) ... where we want to be

Motivation: Teaching ‚NMR data handling‘

- Narrowing it down: Organic (small) molecules
- Impact of teaching: Not only on data quality, but also on publication (quality etc.)...
- Way of teaching: At which point, topics, instruments, and - who teaches?

The educational side

- Teaching (1): Contents transmitted (hands-on training, exercises, theory...)
- Teaching (2): At which point of chemist‘s career (undergraduate, graduate, never...)

Current state - ‚education'

- Teaching: At undergrad level (survey G-NMR 2014),[1] interpretation emphasis on 1D, 2D secondary, theory and exams (ca. 15 hrs), hands-on automation (‚Praktikum', 1D)

- Proficiency at PhD level: ‚Good' (survey IDNMR 2016),[2] 2D experiments standard, published data fully assigned (>50%), assignment on paper (majority)

[1] G-NMR network, www.g-nmr.de
[2] IDNMR project, www.idnmr.uni-koeln.de

The data side

- ‚Data': Digital raw data, not machine-readable assignment, (recently) also electronic export format[1]
- Workflow: Processing (‚automatic'), assignment (manually) - and (usually) no quality control for result

[1] M. Pupier, J.-M. Nuzillard, J. Wist, et al. *Magn Reson Chem*. **2018**, *56*, 703– 715; DOI: 10.1002/mrc.4737.

Current state - ‚technical‘

- Experiments: Actually in use (1D ^{1}H & ^{13}C) vs. available ones (2D ed. HSQC & HMBC)
- Tools: Processing, assignment mainly with proprietary software, free tools for quality control (COCON, CSEARCH, LSD, nmrshiftdb), rarely LIMS with repository

Proposals - ‚at the heart of teaching‘

- Central point is to **teach electronic assignments** (leading to NMReDATA files)
- Prioritize use and interpretation of **2D experiments** (even against ‚organic traditions‘)[1]
- Making the meaning of NMR data clear (‚the eye of the chemist‘)

[1] J.C. Liermann, N.E. Schlörer, *Magn. Reson. Chem.* **2017**, 56, 513-519; DOI: 10.1002/mrc.4675.

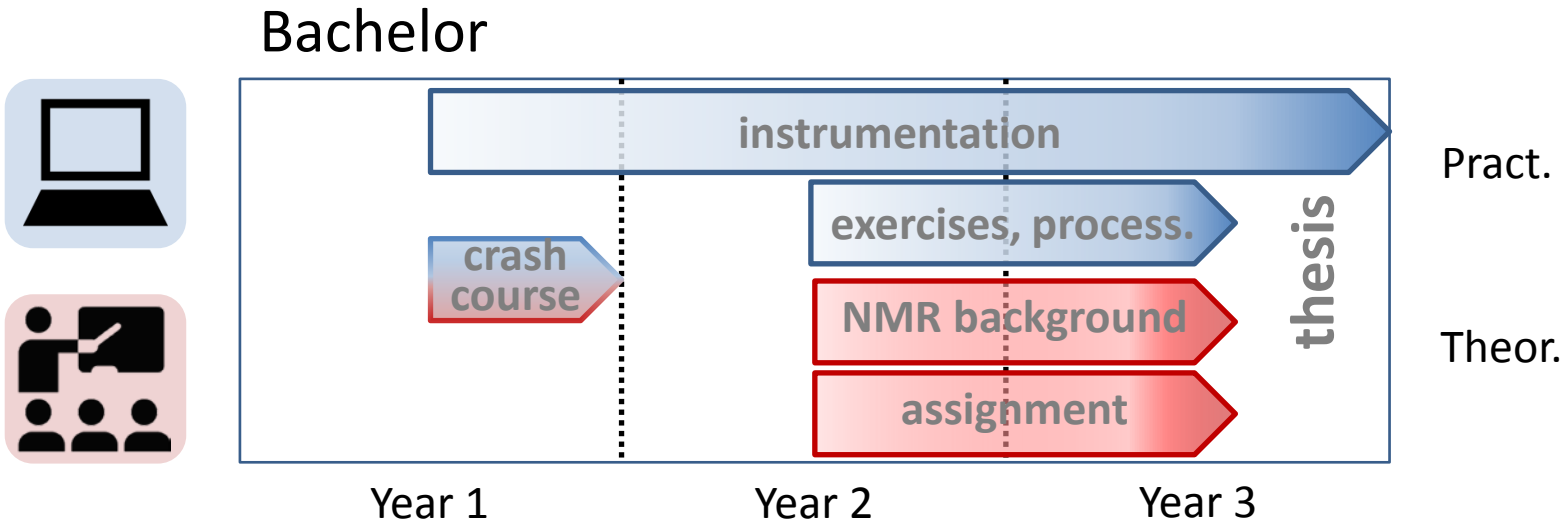
Teaching: Examples, experiences & thoughts

- Local environment: About 150 scientific users (≥MSc), practical lab courses (150 p.a.), 6 magnets (3 open access, 3 operator)
- Lab organisation: Local repository (nmrshiftdb)[1] with LIMS[2] (user & spectrometer management), only free software (€, Spinworks/TopSpin)

[1] C. Steinbeck, S. Krause, S. Kuhn, *J. Chem. Inf. Comp. Sci.* **2003**, *43*, 1733-1739; DOI: 10.1021/ci0341363.
[2] S. Kuhn, N.E. Schlörer, *Magn. Reson. Chem.* **2015**, *53*, 582-589; DOI: 10.1002/mrc.4263.

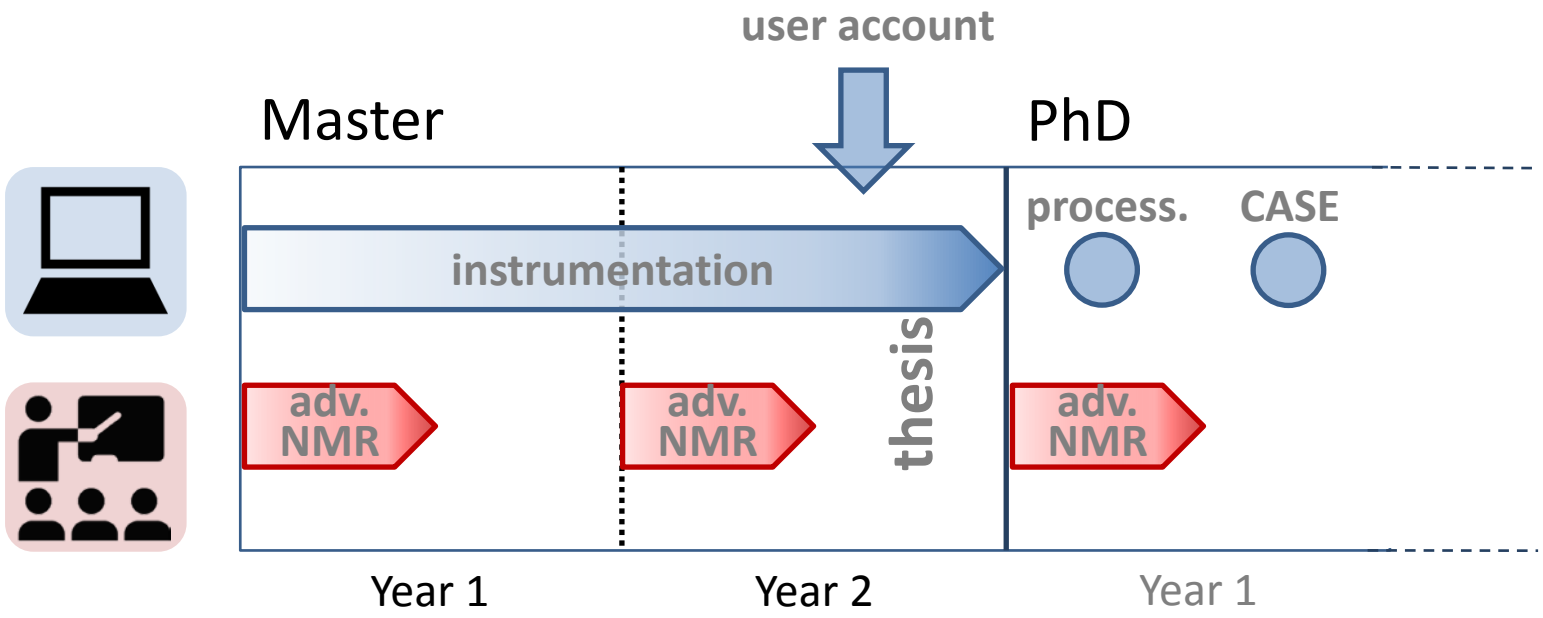
Teaching @ University of Cologne

- Undergraduate: Instrument handling (o.a. use for ‚Praktikum' 3x), basic (1D) spectra processing, NMR theory (class 20 h, exercises 20 h), assignment tools/quality evaluation (nmrshiftdb)



Teaching @ University of Cologne

- Graduate: Advanced NMR class (15 h - optional), intro NMR facility (each user), processing software (1 p.a.), CASE (1 p.a.)



Teaching NMR assignments @ UoC

- Approach: Core of HSQC/HMBC and ^{1}H (additionally COSY, NOE, X nuclei) – on paper and with CASE
- Tools: Local database (nmrshiftdb[1]) to demonstrate evaluation of assignments, CASE (CMCse) = archive format (NMReDATA)

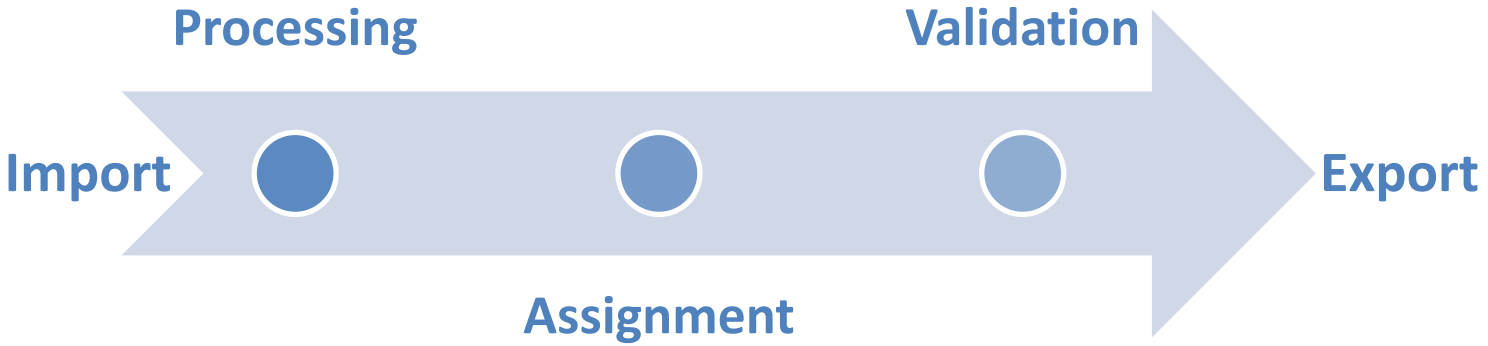
[1] www.nmrshiftdb.org

...where we want to be

- Experimental: Change to 2D as workhorse experiments (no ‚luxury' today & superior for fast validation), include (electronic) assignment and repository in workflow

- Teaching: Use of ELN or at least LIMS/local repo as ‚minimum condition' for teaching data handling. Early involvement of 2D interpretation, annotation/CASE

Vision of workflow



- IDNMR project: Common effort and collaboration between NMReDATA (Damien), Cheminfo (Luc, Julien), LSD (Jean-Marc) and nmrshiftdb (Stefan)

Take home message

- What is taught: 2D assignment including export as electronic (NMReDATA) file (FAIR data)
- Who teaches: NMR scientists can evaluate contents and impact
- Back to the origin: Data authority back to ‚originators‘ (local repos, NMReDATA)

Acknowledgements

- **NMReDATA**: **Damien Jeannerat**, Stefan Kuhn, Jean-Marc Nuzillard, Pavel Kessler
- **IDNMR**: Johannes Liermann, Stefan Kuhn, Hamed Musallam, Luc Patiny, Julien Wist, Christophe Farès
- **nmrshiftdb**: Stefan Kuhn, Christoph Steinbeck
- **Uni Köln:** NMR staff and institute of organic chemistry
- **Funding:** GDCh (special funding MR division), DFG (IDNMR)

Archive format for NMR data (local)

Structure Elucidation Report nmrshiftdb2

<Name>

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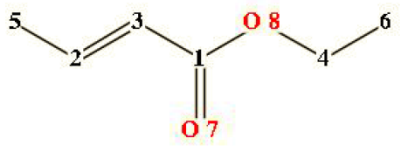


Details

nmrshiftdb2-ID:	<id>
Name:	<name>
Chemical Formula:	C6H10O2
Mass [Da]:	114.1426327741247
Solvent:	CDCl3

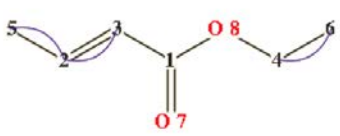
<Comments>

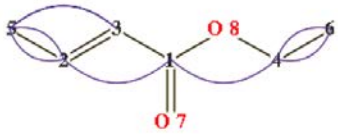
Experimental Details

Experiment Type	ν [Mhz]	Offset [ppm]	Resolution [Hz]	Temperature [K]
1H	500.13			0.0
13C	125.758			0.0
COSY	500.13			0.0
HSQC	500.13			0.0
HMBC	500.13			0.0

Descriptors

SMILES:	C(C=CC)(OCC)=O
INChI:	InChI=1S/C6H10O2/c1-3-5-6(7)8-4-2/h3,5H,4H2,1-2H3/b5-3+
INChI key:	ZFDIRQKJPRINOQ-HWKANZROSA-N





COSY

HMBC

^{13}C table of assignments

Atom	δ [ppm]	Multiplet structure	
		Type	Coupling J [Hz]
1	166.603		
2	144.493		
3	122.699		
4	60.151		
5	17.98		
6	14.166		

^{1}H table of assignments

Atom	δ [ppm]	Multiplet structure	
		Type	Coupling J [Hz]
2	6.949		
3	5.844		
4a	4.177		
5	1.854		
6	1.255		

Archive format for NMR data (local)

Structure Elucidation Report mrshiftdb2 - QuickCheck results

<name>

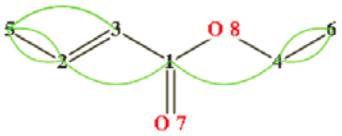
Tue Aug 27 15:59:09 CEST 2019

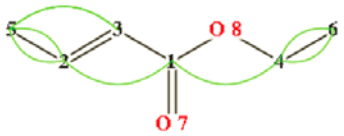
^{13}C assignments

Atom	δ [ppm]	Deviation from prediction
1	166.603	0.30
2	144.493	0.29
3	122.699	0.50
4	60.151	0.15
5	17.98	0.06
6	14.166	0.07

^{1}H assignments

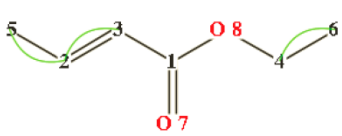
Atom	δ [ppm]	Deviation from prediction
2	6.949	0.04
3	5.844	0.02
4a	4.177	0.02
5	1.854	0.07
6	1.255	0.01

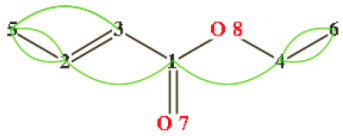




Overall mark 10 (out of 1 to 10, 10 being best)
Mean deviation from prediction: 0.23 ppm ? 0.11 Points
No. of red or missing shifts: 0.0 ? 0.0 Points
No. of yellow shifts: 0.0 ? 0.0 Points

Overall mark 10 (out of 1 to 10, 10 being best)
Mean deviation from prediction: 0.03 ppm ? 0.02 Points
No. of red or missing shifts: 0.0 ? 0.0 Points
No. of yellow shifts: 0.0 ? 0.0 Points





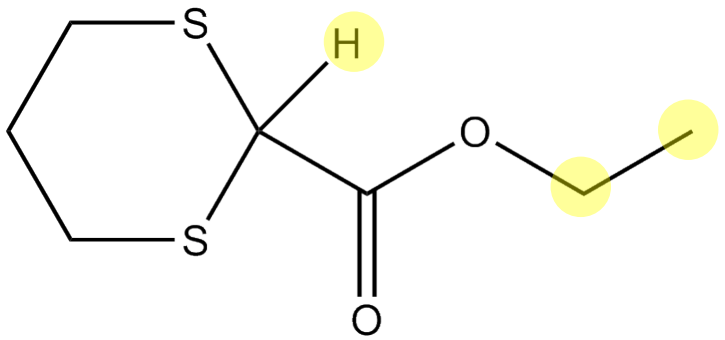
3 of your peaks match expected peaks. There are no peaks in your spectrum not expected, and there are no expected shifts not found in your spectrum.

8 of your peaks match expected peaks. There are no peaks in your spectrum not expected, and there are 3 expected shifts not found in your spectrum.

Overall mark 2D: 8

Assignment format for NMR spectra (1)

- IUPAC recommendation from 1972, applied for publication of NMR data in 1975...



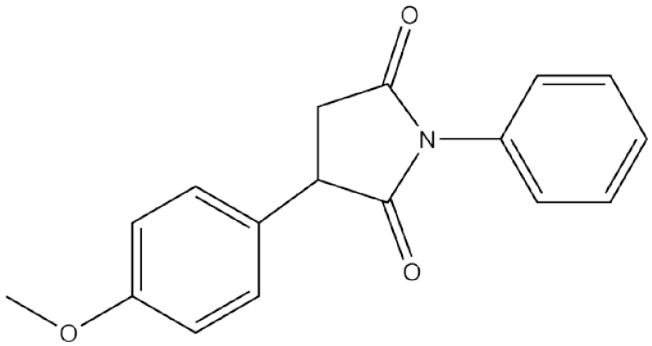
(neat) 3.38, 5.77, 7.06, 7.36, 7.80, 8.78, and 9.74 μ; nmr (CCl_4) 5.98 (s, 2-dithiane H), 5.84 (q, J = 7.0 Hz, ethyl CH_2), 8.71 (t, J = 7.0 Hz, ethyl CH_3). *Anal.* Calcd for $C_7H_{12}O_2S_2$: C, 43.75; H, 6.29.

[Seebach/Corey, *J. Org. Chem.* **1975**, *40*, 231]

Assignment format for NMR spectra (2)

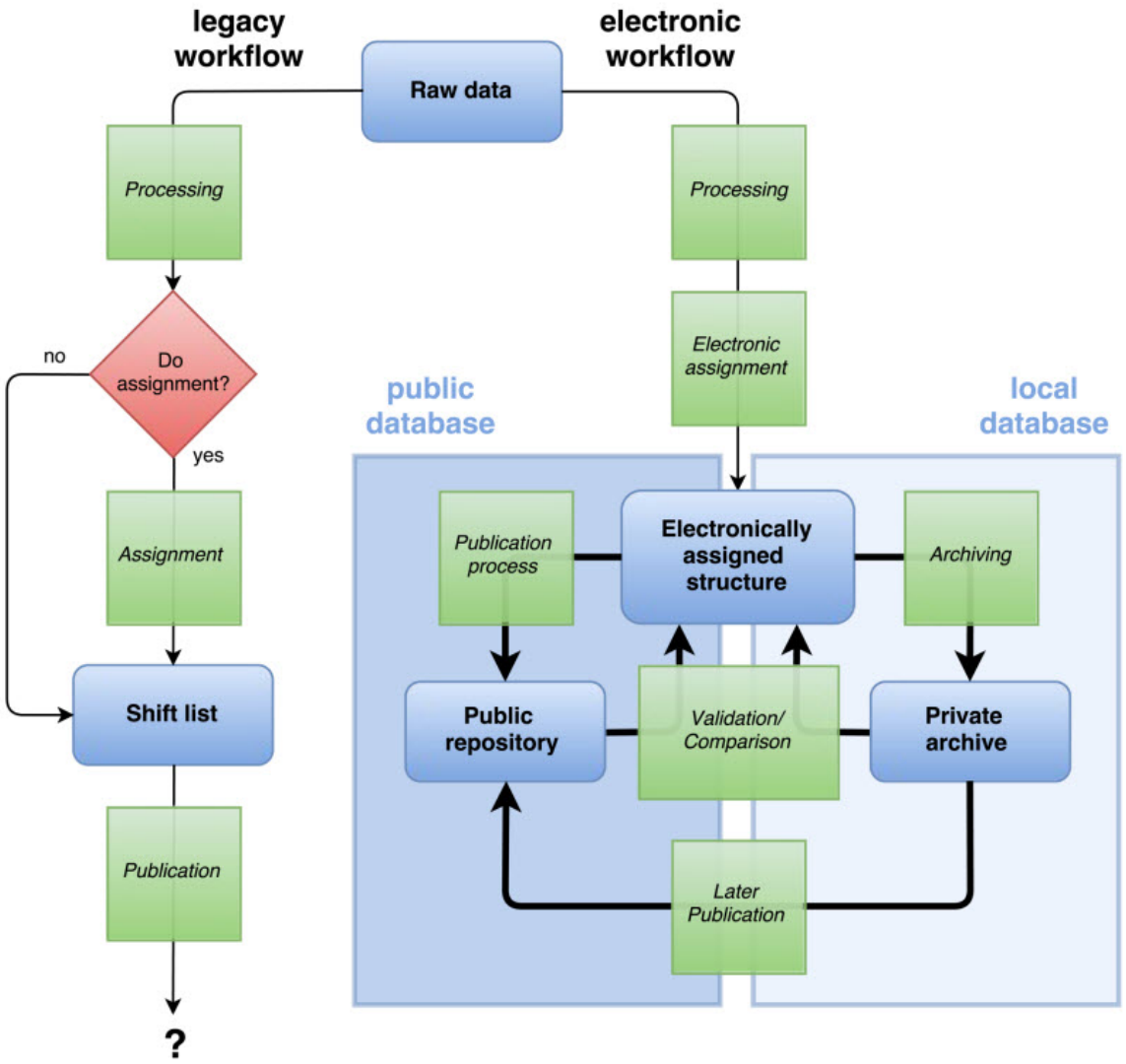
- IUPAC recommendation from 1972, applied for publication of NMR data in 2015...

[Dyson, *J. Org. Chem.* **2015**, *80*, 386]



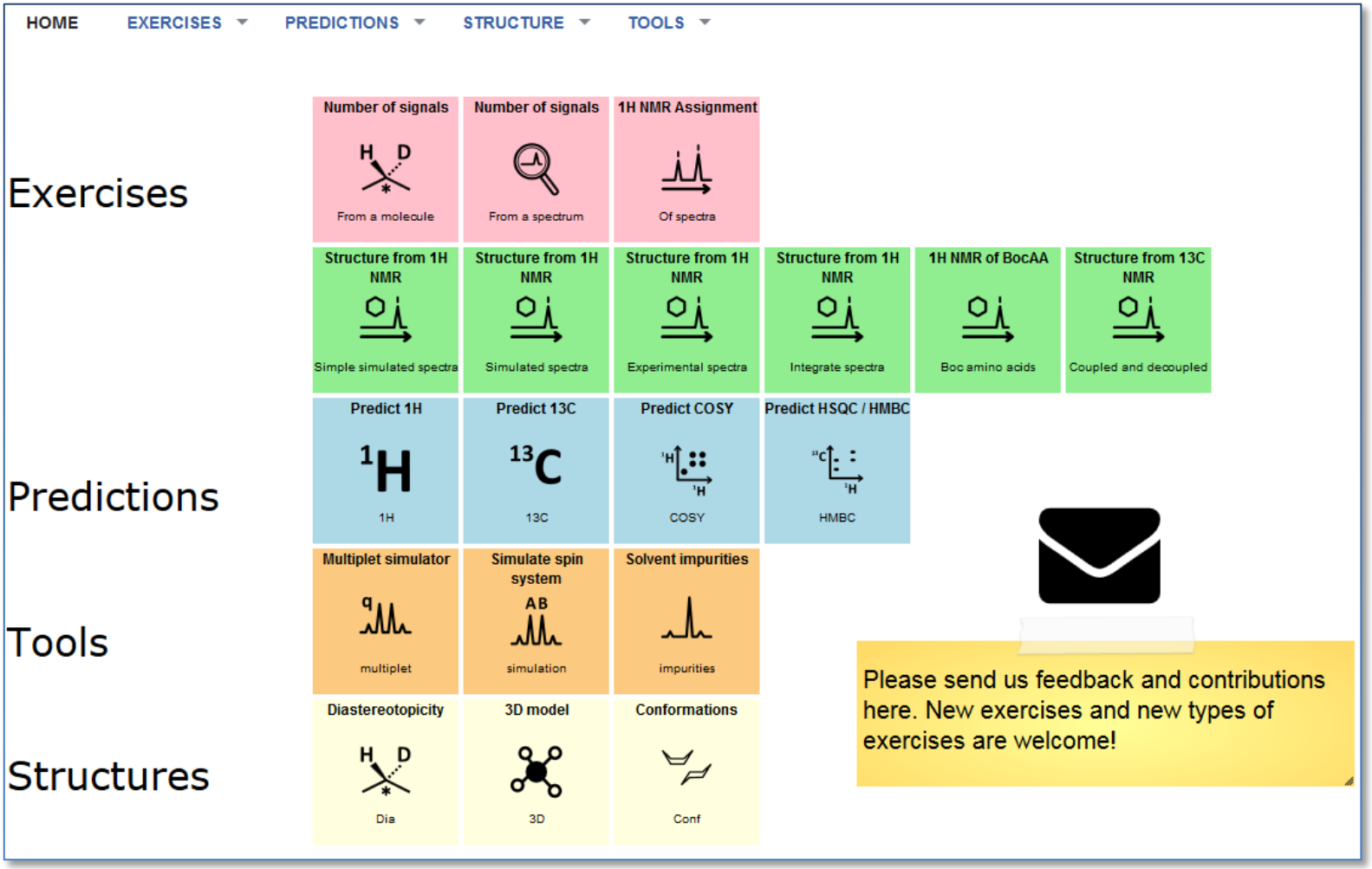
White solid (297 mg, 93% yield): mp 170–173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.47 (m, 2H), 7.46–7.40 (m, 1H), 7.38–7.33 (m, 2H), 7.29–7.24 (m, 2H), 6.99–6.93 (m, 2H), 4.18 (dd, J = 9.7, 4.8 Hz, 1H), 3.85 (s, 3H), 3.40 (dd, J = 18.5, 9.7 Hz, 1H), 3.01 (dd, J = 18.6, 4.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 175.2, 159.3, 132.0, 129.2, 129.0, 128.7, 128.4, 126.5, 114.7, 55.4, 45.3, 31.1.

Workflow for NMR data



J.C. Liermann, N.E. Schlörer, *Magn. Reson. Chem.* **2017**;1–7. DOI 10.1002/mrc.4675

C6H6-Repository: Toolbox for Teaching



L. Patiny, M. Zasso, D. Kostro et al., *Magn. Reson. Chem*. **2017**;1–9. DOI 10.1002/mrc.4669.