

### 3.4 Nuclear Magnetic Resonance (NMR) (C. Farès)

The NMR department provides a broad range of specialised NMR techniques and analytical service for the entire institute. During the reporting period, approximately 60,000 NMR spectra have been recorded on a wide range of samples, going from organic and organometallic compounds in solution to porous silicas and zeolites in solids. To meet demands, the department is equipped with six NMR spectrometers with field strengths corresponding to  $^1\text{H}$  frequencies of 300, 400, 500 and 600 MHz for analyses in solution and of 300 and 500 MHz for analyses in solid state. The department is also staffed with technical and scientific co-workers, skilled in NMR setup and interpretation as well as in related soft- and hardware maintenance. The department is organised in four areas of service.

#### (1) NMR in Full Automation (W. Wisniewski, M. Kochius)

Basic NMR measurements in liquid state can be carried out in high-throughput mode on a dedicated “open access” 300-MHz NMR spectrometers at room temperature. With minimal setup, scientific personnel from the entire institute can access this instrument around the clock and obtain NMR data which are acquired and processed fully automatically. The selection of available experiments is limited to those with high sensitivity, high information content and rapid execution with predefined parameters. These include experiments for 1D spectra of  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  and  $^{11}\text{B}$ . This service covers nearly 90% of all experiments run in our department.

#### (2) Routine NMR (W. Wisniewski, M. Kochius)

Liquid samples requiring special setup or treatment are submitted for measurement to our operators on a 400-MHz spectrometers. The most common requests are for (a) experiments or nuclear frequencies not available in the automatic mode, (b) experiments at high or low temperature, (c) advanced techniques requiring optimisation of acquisition parameters, and (d) spectroscopy of chemical reactions and kinetics followed in real time directly in the NMR tube.

#### (3) Advanced NMR Analyses (C. Wirtz, B. Gabor, P. Philipps, D. Bartels)

Particularly challenging NMR studies of solution compounds are accepted for advanced analysis. For these samples, our experienced staff members provide full measurement, analysis and interpretation assistance in close collaboration with the chemical research groups. The advanced techniques are carried out on one of our two dedicated

spectrometer: (a) a 600-MHz system, equipped with a cryogenically-cooled probehead, which provides exquisite sensitivity and resolution for  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{15}\text{N}$  measurements near room temperature and which is ideally suited for sub-milligram quantities of 50+ carbon organic molecules; (b) a more versatile modern 500-MHz instruments which provides the possibility to measure at high and low temperature, to cover a broad range of NMR-active isotopes, and to run advanced triple-resonance experiments. A large part of the analytical work is dedicated to determine or confirm structures, stereochemistries, conformations and dynamics. Highlights of the departments joint projects are listed here:

- The full spectroscopic characterisation of reaction products during the novel synthesis campaign of natural products, through a rigorous complete  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{15}\text{N}$  assignments. Recent projects accompanied the syntheses of Spirastrellolides Methyl Ester (A and F), Ecklonialactones (A, B and C), Leiodolide B, Tulearin C, and Amphidinolide F (Fürstner group).
- The use of unusual long-range  $J_{\text{HN}}$  couplings to help identify novel carbene-stabilized N-centered cations (Alcarazo group).
- The characterisation of intermediates in palladium-catalysed allylic substitution reaction in four-membered cyclic systems (Maulide group, Fig 1).

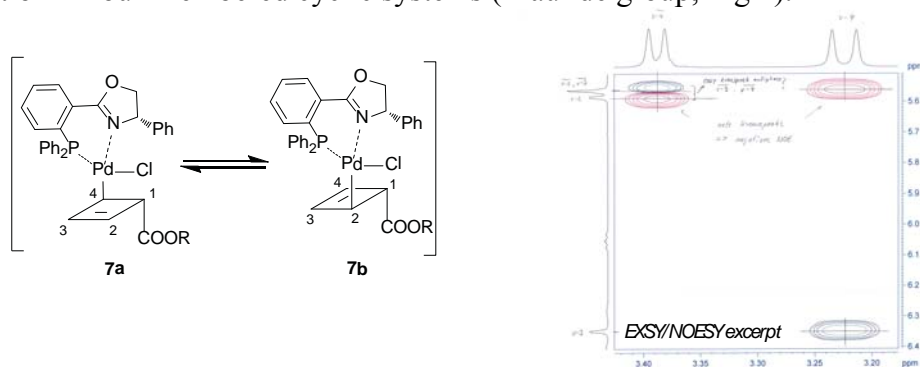


Fig 1 EXSY/NOESY of the Pd-complexed intermediate showing the dynamic exchange process in the cyclobutene ring

- The detection of key players in a Cu-catalysed aerobic oxidative coupling catalytic cycle (Klußmann group, Fig 2)

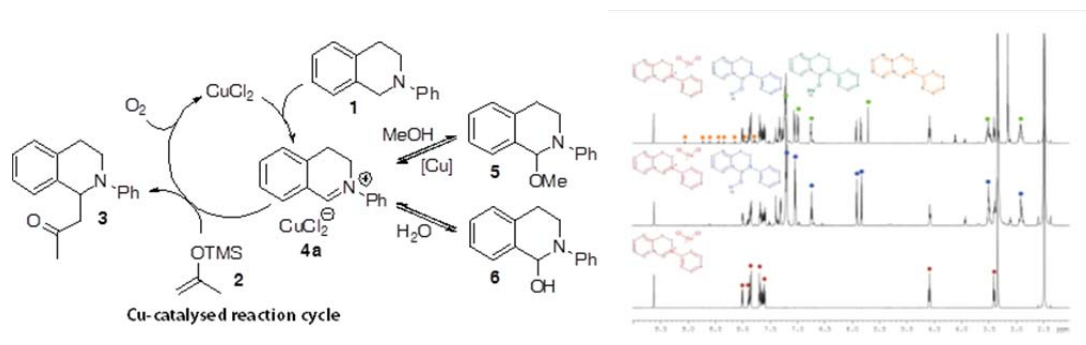


Fig 2  $^1\text{H}$  NMR assignment of the exchanging species present during the Cu-catalysed aerobic oxidative coupling reaction.

- NMR kinetic and mechanistic study in a sulphur-mediated  $\alpha$ -arylation reaction (Maulide group, Fig 3).

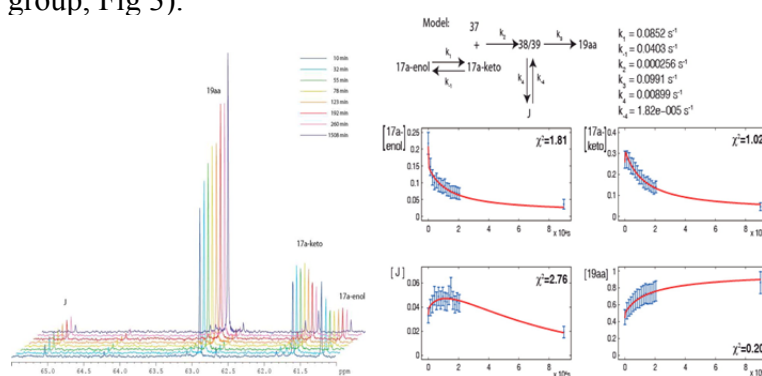


Fig 3: Kinetic profile for the direct sulfoxide-mediated arylation reaction.

- The full structural characterisation and NMR conformation of a key intermediate in primary amine-catalysed asymmetric epoxidation by NMR
- The determination of NMR fingerprint parameters to quickly determined stereochemistry in functionalised dienes (Maulide group).

#### (4) Solid-State NMR (B. Zibrowius)

Solid-state NMR spectroscopy remains one of the most important techniques for the characterisation of solid catalysts and other new materials synthesised in the institute (Schüth group). Both dedicated 300- and 500-MHz spectrometers are equipped with magic-angle spinning (MAS) probeheads to obtain high resolution signals from a wide range of NMR active nuclei. In continuation of work performed in previous years, solid-state NMR spectroscopy has particularly been applied in the following fields:

- Characterisation of solid catalysts prepared from mesoporous silicas or zeolites ( $^{29}\text{Si}$ ,  $^{13}\text{C}$  and  $^{27}\text{Al}$ )

- Detailed studies of various complex aluminium hydrides and boron hydrides (mainly by  $^{27}\text{Al}$  and  $^{11}\text{B}$  NMR, respectively)
- Mechanistic studies on the dehydrogenation process in sodium alanate ( $^{27}\text{Al}$  and  $^{23}\text{Na}$ ).

In addition to these applications, the method has repeatedly been used to contribute to the characterisation of the following materials:

- Organic polymers synthesized as precursors for solid catalysts ( $^{13}\text{C}$  and  $^{31}\text{P}$ )
- Solid products obtained in valorisation processes of wood and lignin ( $^{13}\text{C}$ ).

### Advanced Methods

The NMR department continues to develop and to establish advanced NMR methodologies as part of their collection of routine applications in order to meet the scientific requirements of the institute. A number of newly applied state-of-the-art methods that have been explored and used in the NMR department during the current reporting period.

- Residual dipolar couplings (RDC) to determine stereochemistries, to differentiate enantiomers and to provide complementary conformational and dynamic information.
- *Para*-hydrogen induced polarisation (PHIP) to follow the course of hydration reactions and to identify low amounts of intermediates.
- qNMR and DOSY to characterise and quantify the composition of complex reaction mixtures.
- Novel NMR methods to accelerate (non-uniform sampling (NUS) and ultrafast NMR) and simplify (Pureshift) multidimensional NMR and in order to better follow reactions in real-time.
- Rapid injection NMR (RINMR) for tracking catalytic transformations in “real time”.

### Publications resulting from this research area

- (1) Souris, C.; Luparia, M.; Frebault, F.; Audisio, D.; Farès, C.; Goddard, R., *Chem. - Eur. J.* **2013**, 19, 6566-6570.
- (2) Souris, C.; Frebault, F.; Audisio, D.; Farès, C.; Maulide, N. *Synlett* **2013**, 10, 1286-1290.

- (3) Lifchits, O.; Mahlau, M.; Reisinger, C. M.; Lee, A.; Farès, C.; Polyak, I. *J. Am. Chem. Soc.* **2013**, 135, 6677-6693
- (4) Kozma, A.; Gopakumar, G.; Farès, C.; Thiel, W.; Alcarazo, M. *Chem. - Eur. J.* **2013**, 19, 3542-3546.
- (5) Kondoh, A.; Arlt, A.; Gabor, B.; Fürstner, A. *Chem. - Eur. J.* **2013**, 19, 7731-7738.
- (6) Huang, X. L.; Patil, M.; Farès, C.; Thiel, W.; Maulide, N. *J. Am. Chem. Soc.* **2013**, 135, 7312-7323.
- (7) Audisio, D.; Gopakumar, G.; Xie, L. G.; Alves, L. G.; Wirtz, C.; Martins, A. M. *Angew. Chem., Int. Ed.* **2013**, 52, 6313-6316.
- (8) Arlt, A.; Benson, S.; Schulthoff, S.; Gabor, B.; Fürstner, A. *Chem. - Eur. J.* **2013**, 19, 3596-3608.
- (9) Klimczyk, S.; Huang, X. L.; Farès, C.; Maulide, N. *Org. Biomol. Chem.* **2012**, 10, 4327-4329.
- (10) Andresen, C.; Helander, S.; Lemak, A.; Farès, C.; Csizmok, V.; Carlsson, J. *Nucleic Acids Res.* **2012**, 40, 6353-6366.
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- (12) Lemak, A.; Gutmanas, A.; Chitayat, S.; Karra, M.; Farès, C.; Sunnerhagen, M. *J. Biomol. NMR* **2011**, 49, 27-38.
- (13) Lehr, K.; Mariz, R.; Leseurre, L.; Gabor, B.; Fürstner, A. *Angew. Chem., Int. Ed.* **2011**, 50, 11373-11377.
- (14) Larivee, A.; Unger, J. B.; Thomas, M.; Wirtz, C.; Dubost, C.; Handa, S. *Angew. Chem., Int. Ed.* **2011**, 50, 304-309.
- (15) Hickmann, V.; Kondoh, A.; Gabor, B.; Alcarazo, M.; Fürstner, A. *J. Am. Chem. Soc.* **2011**, 133, 13471-13480.
- (16) Felderhoff, M.; Zibrowius, B. *Phys. Chem. Chem. Phys.* **2011**, 13, 17234-17241.
- (17) Boess, E.; Sureshkumar, D.; Sud, A.; Wirtz, C.; Farès, C.; Klussmann, M. *J. Am. Chem. Soc.* **2011**, 133, 8106-8109.
- (18) Beckmann, U.; Eichberger, E.; Rufinska, A.; Sablong, R.; Klaui, W. *J. Catal.* **2011**, 283, 143-148.
- (19) Benson, S.; Collin, M. P.; Arlt, A.; Gabor, B.; Goddard, R.; Fürstner, A. *Angew. Chem., Int. Ed.* **2011**, 50, 8739-8744.