## 2.2 Department of Homogeneous Catalysis

**Director:** Benjamin List (born 1968)
Publications: 74, 110, 166, 200, 201, 261, 288, 297, 312, 313, 314, 325, 326, 332, 373, 398, 473, 475, 479, 484, 485, 491, 492, 493, 549, 550, 554, 555

**Further group leaders:**

Martin Klußmann (born 1974)
*joined the Institute in January 2007*
Publications: 411, 412, 467

Klaus Jonas (born 1941)
*retired from the Institute in December 2006*
Publication: 413

Klaus-Richard Pörschke (born 1949)
Publications: 2, 35, 359, 379, 413, 428, 429

## Curriculum Vitae: Benjamin List

| | |
|---|---|
| 1968 | Born in Frankfurt, Germany |
| 1993 | Chemistry Diplom, Free University Berlin |
| 1997 | PhD, University Frankfurt |
| 1997-1998 | Postdoc, Scripps Research Institute, La Jolla, USA |
| 1999-2003 | Assistant Professor (Tenure Track), Scripps Research Institute, La Jolla, USA |
| 2003-2005 | Group Leader at the Max-Planck-Institut für Kohlenforschung |
| 2004 | Honorary Professor at the University of Cologne |
| 2005 | Director at the Max-Planck-Institut für Kohlenforschung |

*Awards and Honors*

| | |
|---|---|
| 2000 | Synthesis-Synlett Journal Award |
| 2003 | Carl-Duisberg-Memorial Award |
| 2004 | Degussa Prize for Chiral Chemistry |
| 2004 | Lieseberg Prize |
| 2004 | Lecturer Award of the German Chemical Industry Fund |
| 2005 | Visiting Professorship, Gakushuin University, Tokyo, Japan |
| 2005 | Society of Synthetic Chemistry, Japan: 2005 Lectureship Award |
| 2005 | AstraZeneca European Lecturer |
| 2005 | Novartis Young Investigator Award |
| 2006 | JSPS Fellowship, Japan |
| 2007 | OBC Lecture Award |
| 2007 | AstraZeneca Research Award in Organic Chemistry |
| 1999-2007 | ca. 50 Plenary and Name Lectureships |

*Special Activities*

| | |
|---|---|
| 2005- | Co-Editor of *Synfacts* (Thieme) |
| 2005-2011 | Coordination of the DFG Priority Program (SPP1179) “Organocatalysis” |
| 2007- | Member of the editorial advisory board of the Beilstein Journal of Organic Chemistry |

## Research in the Department of Homogeneous Catalysis

The department primarily focuses on the development of new catalysis concepts within the areas of organocatalysis, transition metal catalysis, and, to some extent, biocatalysis. We explore new catalysts, expand the substrate scope of certain catalytic reactions, apply asymmetric catalysis in natural product synthesis and pharmaceuticals synthesis, and study mechanisms of homogeneous catalytic reactions (B. List, K. R. Pörschke, M. Klußmann).

After several years without leader, Professor Benjamin List became the director of the Department of Homogeneous Catalysis in 2005. Since then the department has grown significantly from ca. 15 members to currently more than 40 members overall. In 2006 Professor Klaus Jonas retired from the Institute, and in 2007 Dr. Martin Klußmann has joined the department as a junior group leader.

The group of Professor List continues to develop organocatalysis as a new methodology complementing the already more advanced fields of biocatalysis and transition metal catalysis as a third approach to asymmetric catalysis. The catalysis with small organic molecules, where an inorganic element is not part of the active principle, has become a highly dynamic area in chemical research. The field is still rather young and currently undergoes a massive growth (Figure 1). The List group designs and identifies new principles for the development of organocatalysts, expands the scope of already developed catalysts such as proline, uses organocatalysis in the synthesis of natural products and pharmaceuticals, and also investigates the mechanism by which organocatalysts activate their substrates. Although to a much lesser extent, the group also develops new concepts in the areas of transition metal catalysis and biocatalysis.

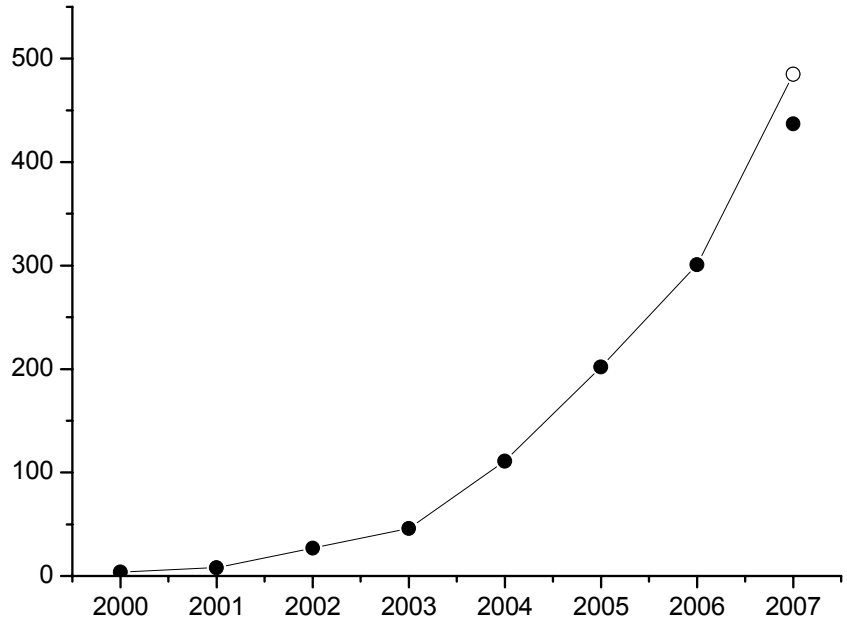



**Figure 1.** Number of publications using the term „organocatalysis“ in the title or abstract since the year 2000 ([●] from SciFinder as of November 21st; second value in 2007 [○] has been predicted).

Research in the laboratory of Professor Pörschke aims at a deeper mechanistic understanding of transition metal catalyzed reactions. Priority is given to the investigation of the structure and reactivity of organometallic compounds relevant to catalytic cycles. A further interdisciplinary project is directed at the investigation of the solid state phase properties of organometallic compounds.

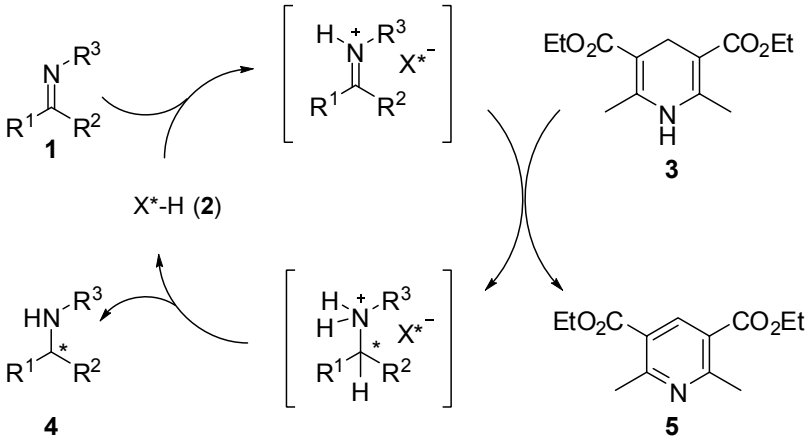
The group of Dr. Klußmann develops new atom economic catalytic reactions and studies the evolution of biological homochirality from a presumably racemic primordial earth.

### 2.2.1 Research Area „Organocatalytic Reduction of Imines / Reductive Amination" (B. List)

**Involved:** S. Hoffmann, A. Majeed Seayad, M. Nicoletti

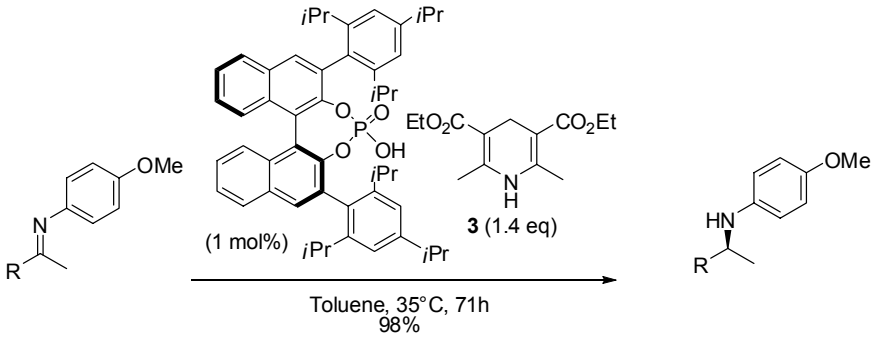
**Objective:** Hydrogenation is arguably the most important catalytic reaction for the synthesis of enantiomerically pure compounds and is crucial for all living organisms.
While effective and industrially relevant catalytic asymmetric hydrogenations and transfer hydrogenations of olefins and ketones have been developed, the corresponding imine reductions although potentially highly useful for the synthesis of enantiomerically pure amines, are less advanced. Asymmetric versions have been realized that require metal-catalysts or the stoichiometric use of metal hydrides. However, the removal of metal-impurities from the reaction product can be difficult but is required in the production of pharmaceuticals because of toxicity concerns.
The aim of this project is the development of a metal-free highly enantioselective transfer hydrogenation of imines. Further, this methodology should be expanded to a reductive amination including a dynamic kinetic resolution of α-branched aldehydes.

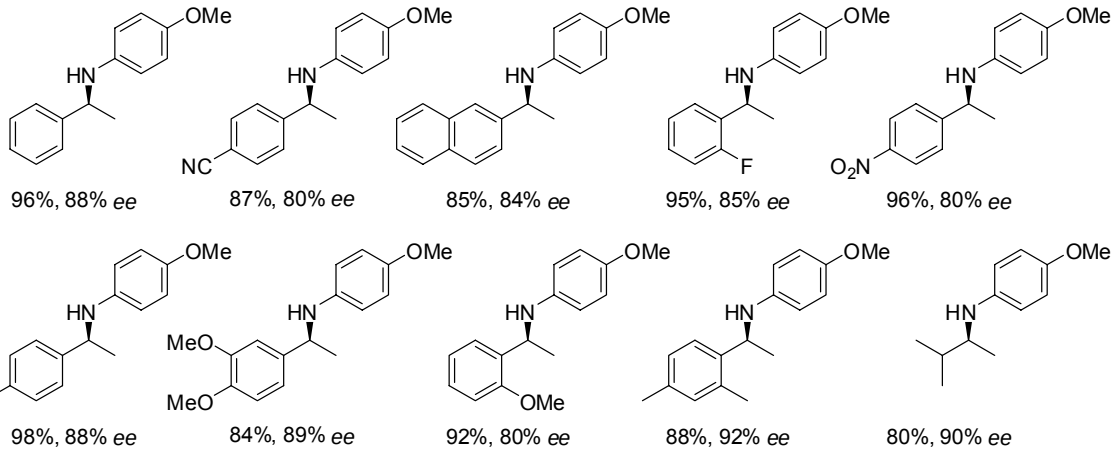
**Results:** Relatively strong chiral phosphoric acids were recently introduced by Akiyama et al. and Terada et al. in pioneering studies as new small organic molecule catalysts for asymmetric addition reactions to aldimines. Inspired by these studies and the observation that imines are reduced with Hantzsch esters in the presence of achiral Lewis- or Brønsted acid catalysts we envisioned a catalytic cycle which is initiated via ketimine (**1**) protonation from a chiral Brønsted acid (**2**) catalyst.




The resulting iminium ion pair, which may be stabilized via hydrogen bonding, is chiral and its reaction with the Hantzsch dihydropyridine **3** could give an enantiomerically enriched amine **4** and pyridine **5**.

As a proof of principle, a commercially available phosphoric acid catalyst clearly showed turnover, giving the product with low enantioselectivity (6% *ee*). Encouraged by these results we synthesized and screened a variety of chiral phosphoric acid catalysts and studied different reaction conditions in the presence of Hantzsch ester **3**. The highest enantioselectivities (up to 93% *ee*) were achieved with only 1 mol% of the new sterically congested phosphoric acid catalyst TRIP. The optimized conditions have been applied to several substituted aromatic ketimines and one aliphatic imine with good to excellent results.

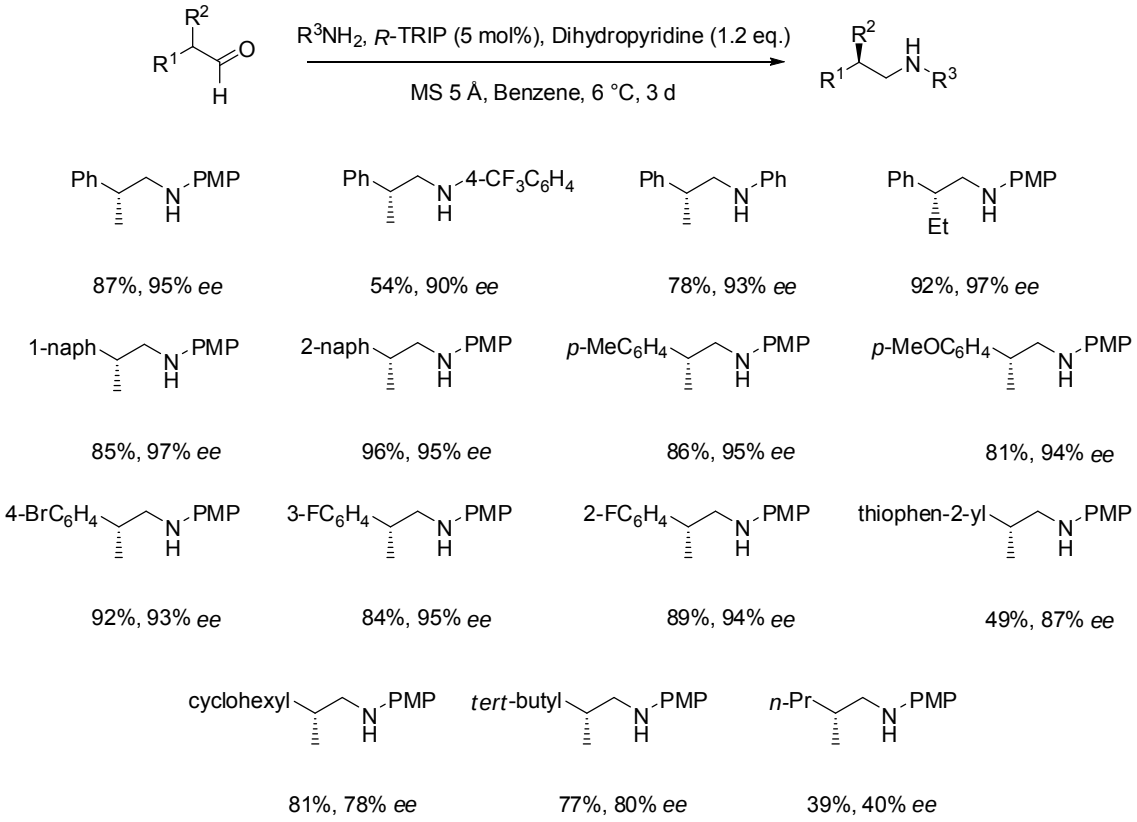



During the preparation of this manuscript a similar study by the group of Rueping using Akiyama's phosphoric acid catalyst appeared.

We hypothesized that under our reductive amination conditions a α-branched aldehyde substrate would undergo a fast racemization in the presence of the amine and acid catalyst via an imine/enamine tautomerization. The reductive amination of one of the two imine enantiomers would then have to be faster than that of the other, resulting in an enantiomerically enriched product via a dynamic kinetic resolution. Although selected asymmetric reductive aminations of ketones to give chiral, α-branched amines

in an enantioface-differentiating process have been reported, the corresponding reactions of α-branched aldehydes to give enriched β-branched amines were unknown. Our optimized protocol was used for the direct reductive amination of both aromatic as well as aliphatic α-branched aldehydes giving good to excellent results.




In summary we have developed an efficient organocatalytic asymmetric ketimine reduction using the chiral phosphoric acid derivative TRIP in the presence of a commercially available dihydropyridine. Additionally, we have reported an efficient enantioselective reductive amination of α-branched aldehydes via dynamic kinetic resolution. Our processes are broad in scope and both aromatic and aliphatic aldehydes can be used.

**Publications resulting from this research area:** 74, 288

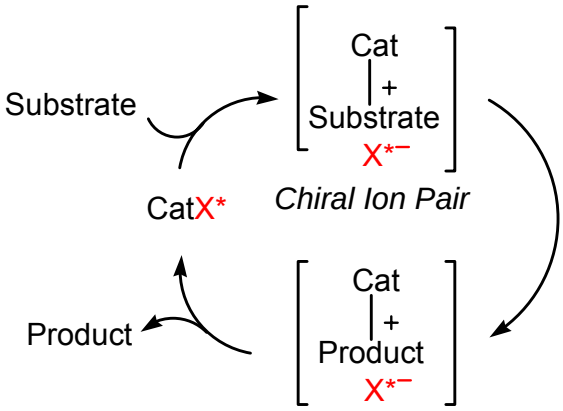
**External funding:** DFG SPP 1179

**Cooperations:** none

### 2.2.2 Research Area „Asymmetric Counteranion-Directed Catalysis (ACDC)" (B. List)

**Involved:** S. Mayer, N. Martin, X. Wang

**Objective:** Most chemical reactions proceed via charged intermediates or transitions states. Such "polar reactions" can be influenced by the counterion. Although efficient asymmetric catalytic transformations involving anionic intermediates with chiral, cationic catalyst have been realized, analogous versions of *inverse* polarity with reasonable enantioselectivity have been elusive, despite several attempts. The aim of this project was to develop a catalytic salts consisting of an achiral but catalytic cation and a chiral phosphate anion for highly enantioselective transformations.

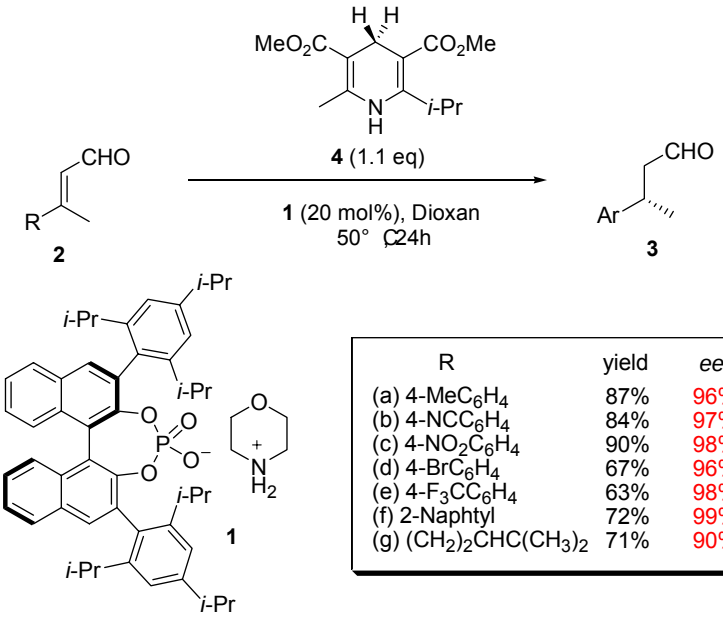



Asymmetric, Counteranion-Directed Catalysis (ACDC)

**Results:** Recently, a metal-free biomimetic transfer hydrogenation of α,β–unsaturated aldehyds was discovered in our research group and independently by MacMillan and coworkers. The reaction is catalyzed by salts of chiral amines and proceeds via iminium ions intermediates in the presence of Hantzsch ester as hydrogen source. Intrigued by the observation of a strong counteranion effect on the yield and enantioselectivity and inspired by the recent introduction of chiral phosphates as asymmetric Brønsted acid catalysts, we hypothesized that catalytic salts of achiral amines and chiral phosphoric acids could induce asymmetry in the process.

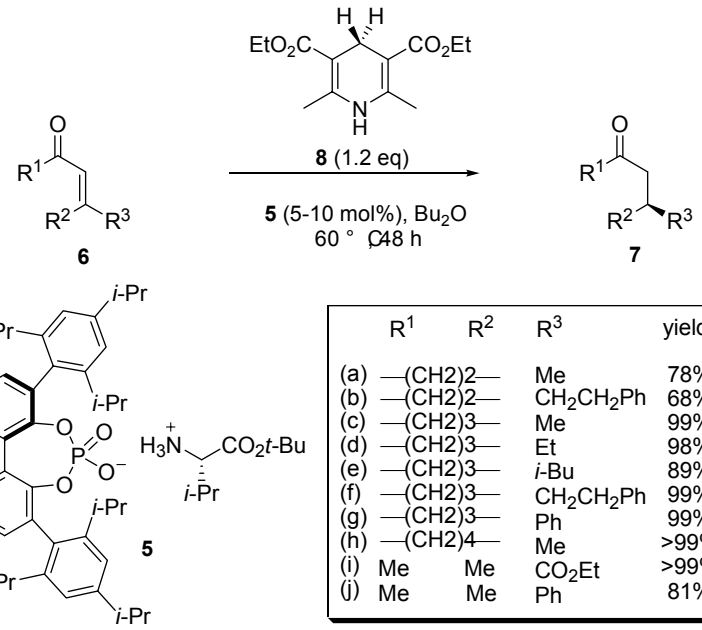
After an extensive screening of several organic salts made of commercially available primary and secondary amines with chiral binaphthol-derived phosphoric acids we found that upon treating trisubstituted α,β-unsaturated aldehydes **2** with a catalytic

amount of morpholine salt **1** and dihydropyridine **4**, the corresponding saturated aldehydes **3** were obtained in high yields and enantioselectivities.




| R | yield | *ee* |
|---|---|---|
| (a) 4-$MeC_6H_4$ | 87% | 96% |
| (b) 4-$NCC_6H_4$ | 84% | 97% |
| (c) 4-$NO_2C_6H_4$ | 90% | 98% |
| (d) 4-$BrC_6H_4$ | 67% | 96% |
| (e) 4-$F_3CC_6H_4$ | 63% | 98% |
| (f) 2-Naphtyl | 72% | 99% |
| (g) $(CH_2)_2CHC(CH_3)_2$ | 71% | 90% |

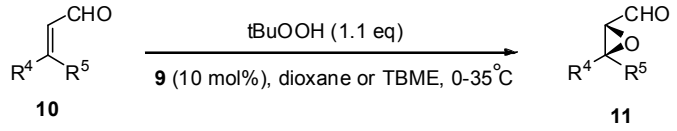
Next, the concept was extended to the transfer hydrogenation of α,β-unsaturated ketones **6** in the presence of a catalytic amount of primary amine salt **5** and dihydropyridine **8** to form the corresponding saturated ketones **7** in high yields and enantioselectivities.

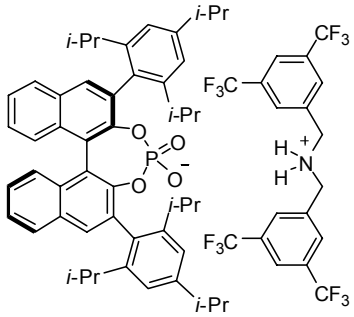



| | $R^1$ | $R^2$ | $R^3$ | yield | *ee* |
|---|---|---|---|---|---|
| (a) | —(CH2)2— | | Me | 78% | 98% |
| (b) | —(CH2)2— | | $CH_2CH_2Ph$ | 68% | 96% |
| (c) | —(CH2)3— | | Me | 99% | 94% |
| (d) | —(CH2)3— | | Et | 98% | 96% |
| (e) | —(CH2)3— | | *i*-Bu | 89% | 95% |
| (f) | —(CH2)3— | | $CH_2CH_2Ph$ | 99% | 96% |
| (g) | —(CH2)3— | | Ph | 99% | 84% |
| (h) | —(CH2)4— | | Me | >99% | 97% |
| (i) | Me | Me | $CO_2Et$ | >99% | 83% |
| (j) | Me | Me | Ph | 81% | 69% |

Catalytic enantioselective epoxidations of olefins have traditionally defined the state of the art in asymmetric catalysis. Very recently, equally elegant and useful

organocatalytic asymmetric epoxidations of α,β-unsaturated aldehydes via iminium catalysis have been developed by Jørgensen et al. We have now identified a new salt (**9**) formed from an achiral ammonium ion and a chiral phosphate anion that catalyzes the highly enantioselective epoxidation of disubstituted aromatic α,β-unsaturated aldehydes (**10a-m**) and also gives excellent enantioselectivities with trisubstituted α,β-unsaturated aldehydes (**10n-q**), which previously have been illusive substrates for any type of highly enantioselective epoxidation.



9

| | $R^4$ | $R^5$ | yield | *dr* | *ee* |
|---|---|---|---|---|---|
| (a) | Ph | H | 75% | >99 : 1 | 91% |
| (b) | 2-naphthyl | H | 76% | >99 : 1 | 95% |
| (c) | 1-naphthyl | H | 70% | 98 : 2 | 91% |
| (d) | 4-Ph-$C_6H_4$ | H | 78% | >99 : 1 | 91% |
| (e) | 4-Me-$C_6H_4$ | H | 65% | >99 : 1 | 92% |
| (f) | 3-Me-$C_6H_4$ | H | 68% | >99 : 1 | 92% |
| (g) | 2-Me-$C_6H_4$ | H | 62% | 97 : 3 | 90% |
| (h) | 4-Cy-$C_6H_4$ | H | 60% | >99 : 1 | 90% |
| (i) | 4-F-$C_6H_4$ | H | 78% | >99 : 1 | 93% |
| (j) | 3-F-$C_6H_4$ | H | 82% | >99 : 1 | 84% |
| (k) | 2-F-$C_6H_4$ | H | 69% | 98 : 2 | 91% |
| (l) | 4-Cl-$C_6H_4$ | H | 84% | >99 : 1 | 87% |
| (m) | 4-Br-$C_6H_4$ | H | 80% | >99 : 1 | 87% |
| (n) | Me | Me | 83% | 95 : 5 | 94% |
| (o) | Et | Et | 85% | -- | 94% |
| (p) | --$(CH_2)_5$-- | Me | 75% | -- | 90% |
| (q) | $(CH_2)_2CHC(CH_3)_2$ | | 95% | 72 : 28 | 76%(*trans*)<br>92%(*cis*) |

In summary, our ACDC concept has been successfully applied to enantioselective organocatalytic conjugate reductions and epoxidations of α,β-unsaturated carbonyl compounds. We are currently extending the concepts to other areas, including transition metal catalysis.

**Publications resulting from this research area:** 325, 326

**External Funding:** DFG SPP 1179

**Cooperations:** W. Thiel (Mülheim/Ruhr, DE)

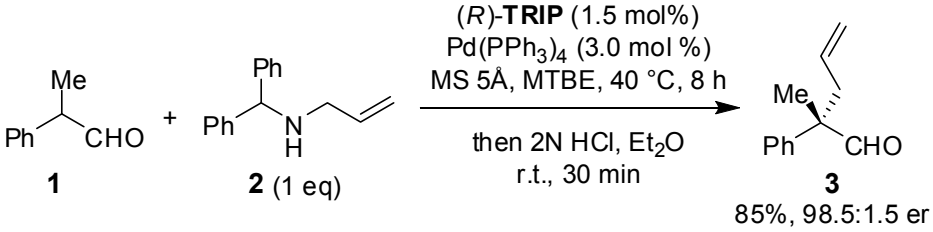
### 2.2.3 Research Area "Asymmetric Direct α-Allylation of Aldehydes" (B. List)

**Involved:** S. Mukherjee

**Objective:** The enantioselective construction of all-carbon quaternary stereogenic centers is a challenging task in organic synthesis. Asymmetric alkylations of α-branched carbonyl compounds constitute an attractive solution to this problem and the palladium-catalyzed asymmetric allylic alkylation has proven particularly useful. However, the asymmetric α-allylation of α-branched aldehydes still remains a considerable challenge. Although recently a few methods have been described for the direct catalytic asymmetric α-allylation of aldehydes, none of these methods allow for the formation of quaternary stereogenic centers. The aim of this project was to develop an efficient and highly enantioselective direct α-allylation of α-branched aldehydes.

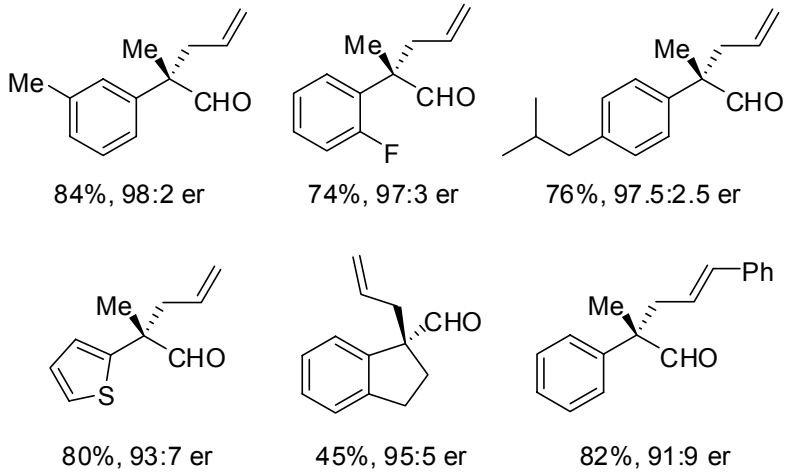
**Results:** We have recently introduced the concept of asymmetric counteranion direct catalysis (*ACDC*) as a new tool in asymmetric catalysis and demonstrated its potential in the enantioselective transfer hydrogenation and the asymmetric epoxydation of enals. However, the application of *ACDC* was so far limited in the domain of organocatalysis. We reasoned that this concept could be applied to organometallic systems as well. To prove this principle we studied the enantioselective direct α-allylation of α-branched aldehydes.

We found that when 2-phenyl propionaldehyde **1** was treated with *N*-benzhydryl allyl amine **2** as the allylating agent in the presence of $Pd(PPh_3)_4$ (3 mol%) and the phosphoric acid co-catalyst **TRIP** (1.5 mol%) under optimized reaction conditions (MS 5 Å, MTBE, 40 °C, 8 h), α-allylated aldehyde **3** was obtained in 85% yield with 98.5:1.5 er after hydrolysis.




We also studied the scope of this enantioselective direct aldehyde α-allylation reaction. A number of differently substituted phenyl and other 2-aryl propionaldehydes were employed as substrates and the products were obtained in good yields (71-89%) and er (93:7 to >98:2). The allylated product of 2,3-dihydro-1-indanone derived aldehyde was

obtained in high er but in moderate yield. Substitution at the 3-position of the allyl group has also been investigated with good results. Currently we are working on to extend the scope of *ACDC* to other metal-catalyzed reactions.




84%, 98:2 er  74%, 97:3 er  76%, 97.5:2.5 er

80%, 93:7 er  45%, 95:5 er  82%, 91:9 er

**Publications resulting from this research area:** 485

**External Funding:** none

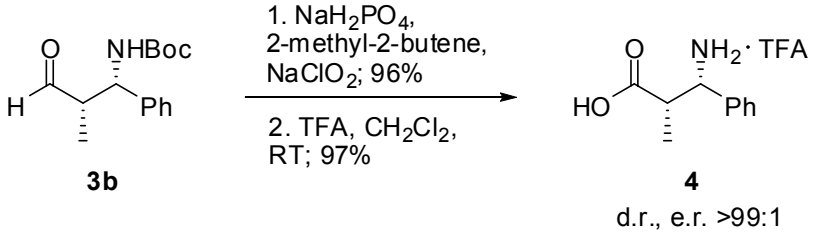
**Cooperations:** none

### 2.2.4 Research Area „Proline-Catalyzed Mannich Reaction of Aldehydes with *N*-Boc Imines" (B. List)

**Involved:** J. W. Yang, M. Stadler

**Objective:** The catalytic asymmetric Mannich reaction is arguably the most useful approach to synthesize chiral β-amino carbonyl compounds. We discovered a proline-catalyzed version of this powerful reaction. Originally, the proline-catalyzed Mannich reaction required the use of anilines as the amine component. Since the N-substituent is usually employed as protecting group, it should be easily removable after the reaction has taken place. However, the removal of the most commonly used *p*-methoxyphenyl (PMP) group from nitrogen often requires drastic oxidative conditions involving harmful reagents such as ceric ammonium nitrate (CAN) that are not compatible with all substrates. We have now employed the *tert*-butoxycarbonyl (Boc)-group as an easily removable protecting group in order to overcome this drawback. The aim of this project has been to develop the efficient, practical, and highly stereoselective Mannich reaction of *N*-Boc imines.

**Results:** We found the reaction of unmodified aldehydes and ketones with simple preformed aromatic *N*-Boc-imines including electron-poor and electron-rich imines to give chiral β-amino aldehydes and ketones in high levels of diastereo- and enantioselectivities. For instance, when the benzaldehyde-derived *N*-Boc-imine **2a** ($R_3$ = Ph) was treated with a two-fold excess of *n*-hexanal in the presence of 20 mol% (*S*)-proline in $CH_3CN$ at 0 °C, the desired product **3a** precipitated and could be collected by filtration (**Fig. 1**) in 84% yield with extremely high diastereoselectivity (>99:1 *dr*) and enantioselectivity (>99:1 *er*). Similarly with most other substrate combinations, the products of the reaction either precipitate from the reaction mixture and can be collected *via* filtration, or are obtained by an aqueous workup/organic extraction process as stable, crystalline solids. Purification of the products can be achieved by trituration with cool hexanes. The *N*-Boc-imine derived Mannich products **3a-g** can readily be converted into the corresponding α,β-branched-β-amino acids **4** ($\beta^{2,3}$-amino acids).




**3b** **4**

d.r., e.r. >99:1

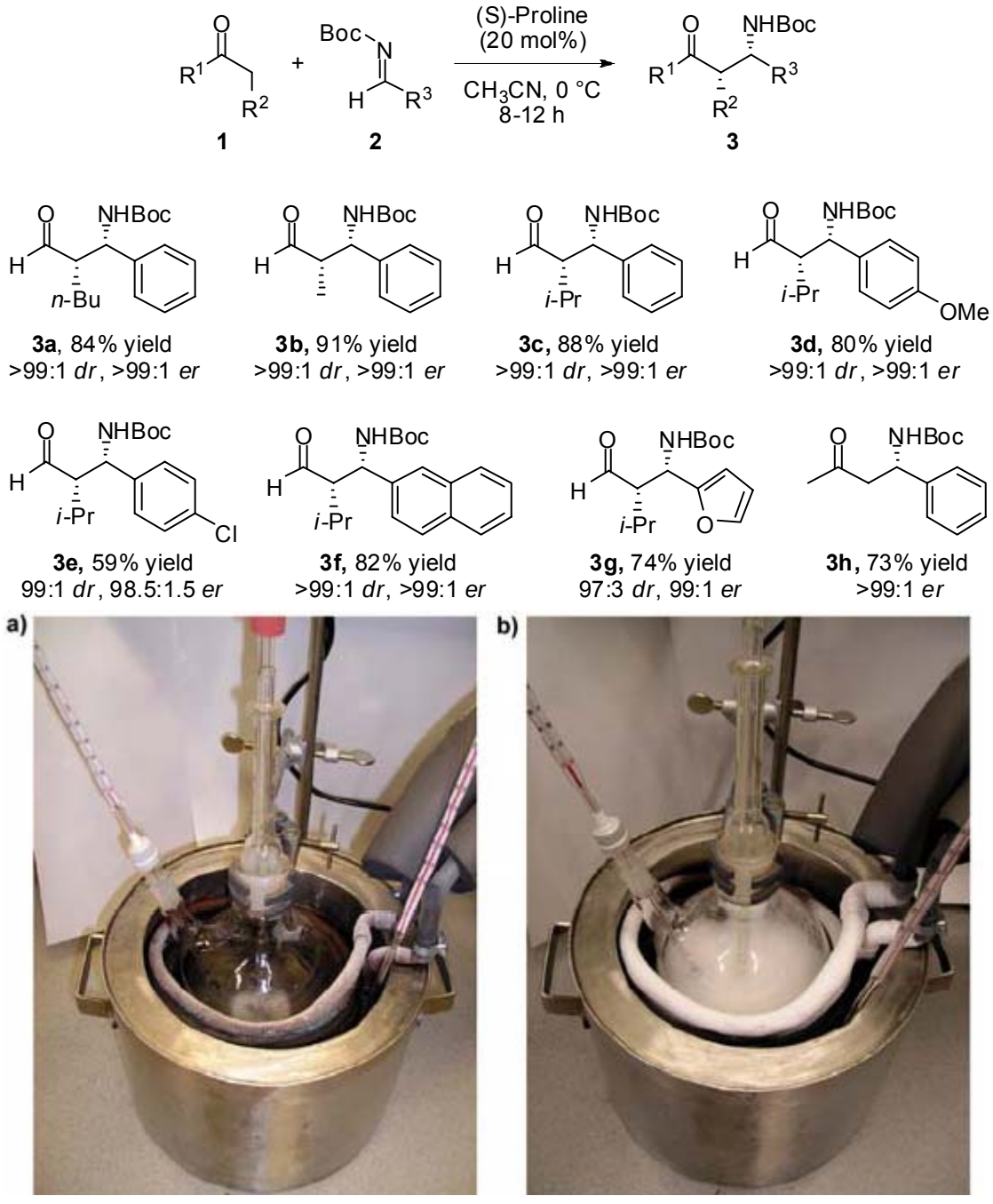



**Fig. 1**: a) Reaction vessel after mixing all compounds; b) Precipitated product after reaction

In summary, we have developed a remarkably efficient and enantioselective variant of the proline-catalyzed Mannich reaction. In our new procedure, aldehydes react with preformed *N*-Boc-imines in the presence of proline to give the corresponding β-amino aldehydes in excellent diastereoselectivities and enantioselectivites.

**Publications resulting from this research area:** 549, 550

**External Funding:** none

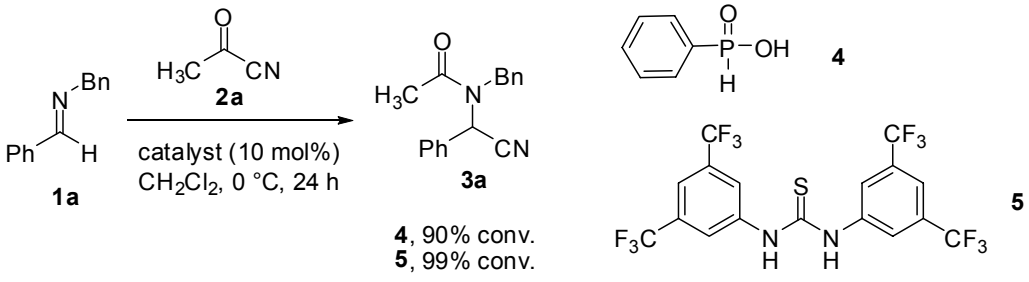
**Cooperations:** none

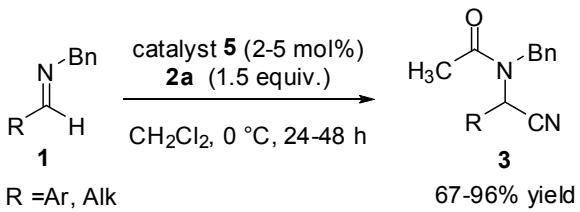
## 2.2.5. Research Area „Catalytic Acylcyanation of Imines" (B. List)

**Involved:** S. C. Pan, J. Zhou

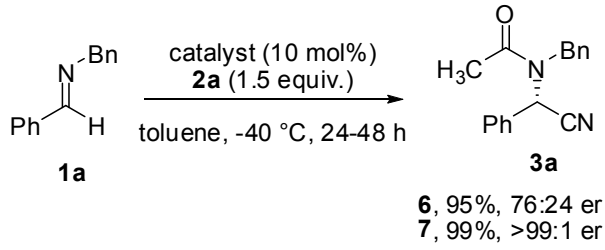
**Objective:** Discovered in 1850, the Strecker reaction has been identified as one of the most efficient methods for the preparation of α-amino nitriles, which are useful intermediates in the synthesis of α-amino acids. In recent years, considerable effort has been devoted toward the development of asymmetric Strecker reactions. Despite rapid progress in this field, volatile and highly toxic HCN has been used in most Strecker variants. On the other hand, acyl cyanides are less toxic and have already been used for the acylcyanation of carbonyl compounds. Surprisingly however, the reaction of acyl cyanides with imines has been significantly less investigated. The aim of this project was to develop a catalytic asymmetric and non-asymmetric acylcyanation of imines. We also intended to develop a three-component variant of the acylcyanation reaction.

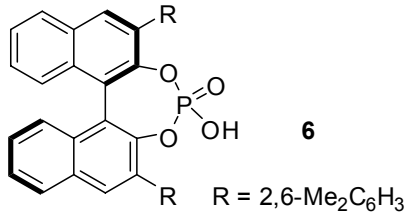
**Results:** Building upon the observations of Dornow and Lüpfert, we initially investigated triethyl amine as catalyst for the reaction of benzaldehyde derived imine **1a** with acetyl cyanide **2a**, however only 4% conversion to the product **3a** was obtained using dichloromethane as the solvent. Reasoning that in addition to base-catalysis, an acid catalyzed pathway should be possible as well, we next investigated different Brønsted acid catalysts to promote the reaction. In fact, moderately acidic phenyl phosphinic acid **4** gave good conversion at 0°C. Finally, hydrogen-bonding-type Schreiner thiourea catalyst **5** was identified to be the best catalyst for the reaction. Decreasing the catalyst loading from 10 mol% to 2 mol% essentially preserved the conversion (98%). With 2-5 mol% of catalyst **5**, the scope of this reaction was studied and 67-96% yield was obtained for different aliphatic and aromatic aldimines.

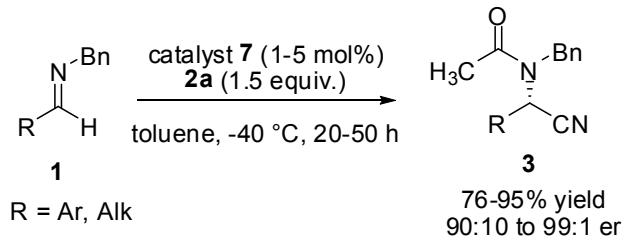


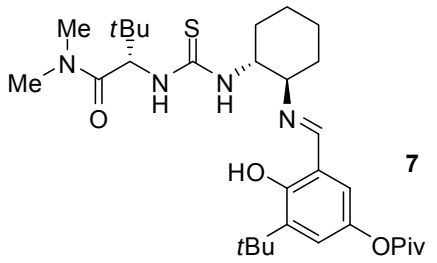



To develop an asymmetric version of this reaction, we initially prepared several chiral binol-derived phosphoric acid catalysts. However, while these catalysts gave *N*-acetylated amino nitrile product **3a** in high yields, enantioselectivities were only moderate. In the best case, the use of catalyst **6** led to **3a** with 79:21 er. We then prepared a range of chiral thiourea catalysts. Remarkably, catalyst **7** gave the product in essentially enantiomerically pure form. In the further optimization, we tried to lower the catalyst loading and found that 1 mol% of catalyst **7** is sufficient to give the product in high yield as well as with excellent enantioselectivity.

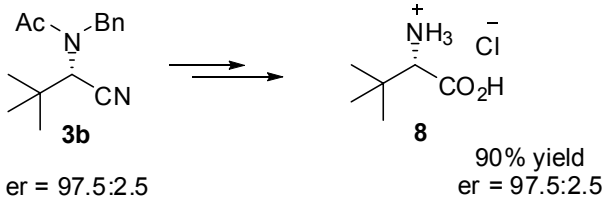


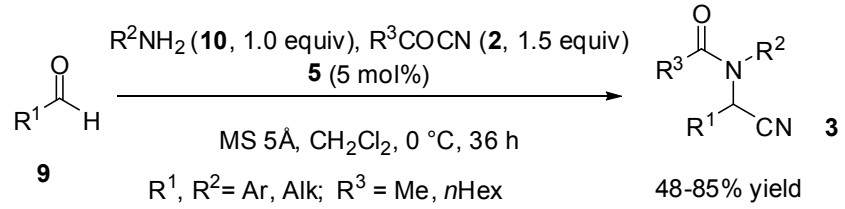




Then, this catalyst has been investigated with a number of different imines and it was found that the reaction gives products in very high enantioselectivities with different aromatic, heteroaromatic, aliphatic and unsaturated aldimines. Noteworthy, high enantioselectivity (98:2 er) have been obtained for the important pivalaldehyde derived imine **1b**. *N*-acylated α-amino nitrile **3b** was converted into *t*-leucine salt **8** via acid mediated hydrolysis and hydrogenolysis without racemisation.

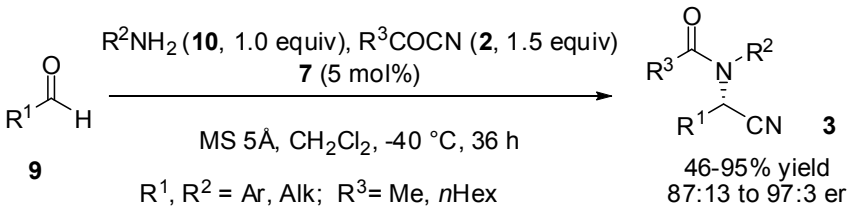



We then started to develop a three-component variant of the acylcyanation reaction. Initially we found that stirring benzaldehyde (**9a**), benzyl amine (**10a**), $MgSO_4$, catalyst **5**, and acetyl cyanide (**2a**) at 0 °C for 24 h in dichloromethane resulted in poor yield of the desired product **3a** and considerable side product formation. In this case, a considerable amount of *N*-benzyl acetamide was formed resulting from the direct reaction of benzyl amine with acetyl cyanide. We envisioned that in order to suppress

this side reaction, the order of reagent mixing may be crucial. Thus, when acetyl cyanide was added last, significant conversion to the desired product could be realized. The best result (99% conv.) was obtained when the mixture of aldehyde, amine, MS 5Å, and catalyst **5** were stirred together at room temperature for 2 h before the addition of acetyl cyanide at 0 °C. After establishing suitable reaction conditions, we decided to explore the scope of this new three-component reaction. Different aldehydes (both aryl and alkyl) and different amines (both benzyl and alkyl) gave the products in moderate to high yields. The third component of our reaction can also be varied. For example, commercially available heptanoyl cyanide gave the product in 72% yield.




We reasoned that extending our acylcyanation methodology to an attractive one-pot three-component catalytic asymmetric acyl-Strecker reaction could be possible. We decided to explore our three-component variant using Jacobsen's thiourea catalyst **7** which gave high enantioselectivities in the analogous preformed imine variant. According to our findings in the non-asymmetric three-component version, we added acetyl cyanide at last to realize efficient conversion to the desired product. Finally, we identified that the best result (98% yield, 97:3 e.r.) was obtained if the aldehyde was first mixed with the amine and MS 5Å for 2 h at r.t. before the catalyst and acetyl cyanide were added subsequently at -40 °C. Under this optimized condition, different aldehydes, amines and acylcyanides were studied and good results were obtained.




Our processes represent the first catalytic asymmetric acylcyanation of imines and the first organocatalytic asymmetric three-component acyl-Strecker reaction.

**Publications resulting from this research area:** 332, 491, 492, 493

**External Funding:** none

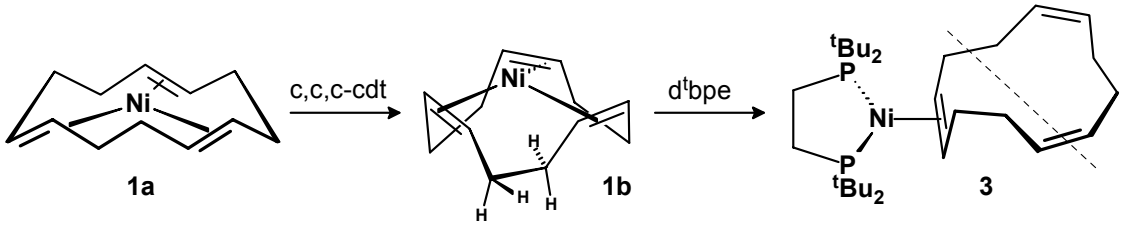
**Cooperations:** none

### 2.2.6 Research area "Coordination Chemistry of Nickel and Palladium" (K.-R. Pörschke)

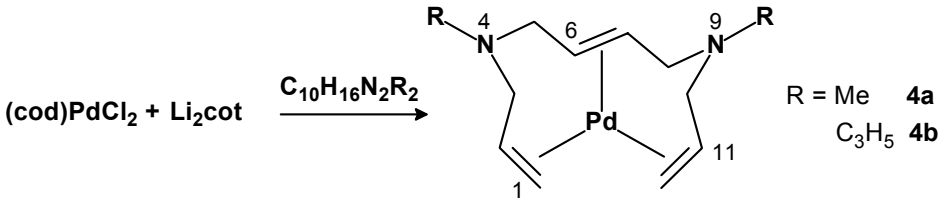
**Involved:** E. Chernyshova, X. Tian, R. Goddard

**Objective:** While many reactions are catalyzed by Ni and Pd compounds, the exact nature of the catalyst is often not clear. (a) We were intrigued to learn more about the properties of "naked nickel" complexes and whether "naked palladium" can also be provided. (b) Furthermore, the species developed from the reaction of $(\eta^3\text{-}C_3H_5)M(L)X$ (M = Ni, Pd; L = phosphane or NHC; X = halide) with AgY (Y = noncoordinating anion) is still under discussion (NHC = *N*-heterocyclic carbene). (c) While *β*-diketiminato ("nacnac") has emerged as an interesting ligand conferring unusual properties to many metals (e.g., Ni), relatively little is known about its coordination chemistry with palladium. The research reported here is intended to shed more light in these areas.

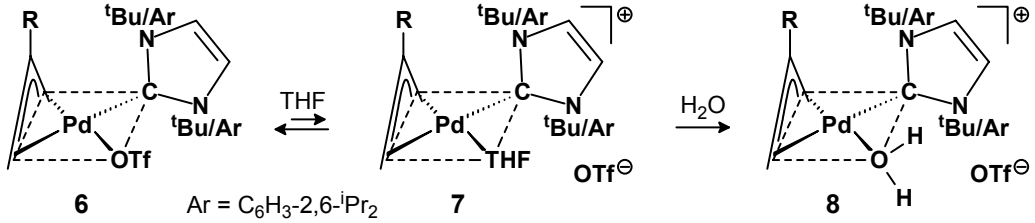
**Results:** (a) As compared to Wilke's famous (t,t,t-cdt)Ni (**1a**) (cdt = 1,5,9-cyclododecatriene) having the three C=C bonds twisted out of the coordination plane, the isomeric (c,c,c-cdt) (**1b**) was suggested to show an in-plane arrangement of the C=C bonds and consequently an improved backbonding. However, although **1b** is formed from **1a**, it is thermally less stable and considerably more reactive with respect to oxidation, aspects which called for a closer inspection of the bonding. A general investigation of the ligand properties of c,c,c-cdt showed that it coordinates to a circumferentially positioned metal in a $C_2$ symmetrical ("helical") conformation and to a central metal in a $C_3$ symmetrical ("ratchet") mode. Rather stable complexes are obtained for a central Cu(I), (c,c,c-cdt)CuX (**2**). While in the latter complexes the three C=C bonds are indeed approximately coplanar, their individual coordination to the metal center is asymmetric, and furthermore, the metal is displaced out of the plane of the C=C bonds. Thus, c,c,c-cdt does apparently not accommodate an ideally trigonally planar coordinated metal atom, and the coordination geometry of a central metal is perforce distorted toward trigonal pyramidal. This explains why backbonding in **1b** is not optimal, and it also explains the observed reactivity of **1b**. According to an X-ray structure analysis, **1b** crystallizes in the trigonal space group $R\bar{3}m$, with one (c,c,c-cdt)Ni moiety in the unit cell. The molecules are disordered and stacked vertically above one another, and the molecules of adjacent columns are close-packed to each other. Reaction of **1b** with a bidentate phosphine leads to displacement of two of the three C=C bonds and formation of complex **3**, in which the c,c,c-cdt ligand has now assumed the helical conformation.




While in t,t,t,-cdt and c,c,c-cdt the three C=C bonds are in a 1,5,9-sequence, it was shown in a further investigation that 1,6,11-trienes are even better suited to coordinate to a $d^{10}$ metal, and here acyclic ligands already confer sufficient stability to the complexes. Thus, while the Pd(0) homologues to **1a,b** are unknown, **4a,b** bearing 4,9-diazadodeca-1,trans-6,11-triene ligands are stable. These Pd(0) complexes, which readily sublime above 50 °C, both represent viable sources for "naked palladium" in solution and also appear suited for vapor deposition techniques.

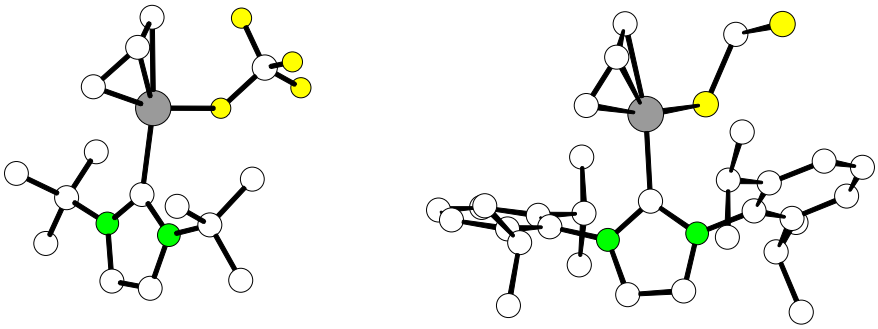



(b) $\{(\eta^3\text{-}2\text{-}RC_3H_4)Pd(\mu\text{-}Cl)\}_2$ (R = H, Me) react with AgOTf to give the polymeric $\{(\eta^3\text{-}C_3H_5)Pd(\mu\text{-}OTf)\}_n$ (**5a**), forming close-packed helical chains in the crystal, and the dimeric $\{(\eta^3\text{-}MeC_3H_4)Pd(\mu\text{-}OTf)\}_2$ (**5b**). Reaction of **5** with NHC (NHC = $C(N(^t\text{Bu})CH)_2$, $C(N(C_6H_3\text{-}2,6\text{-}^i\text{Pr}_2)CH)_2$) affords the so far elusive triflates $(\eta^3\text{-}2\text{-}RC_3H_4)Pd(NHC)(OTf)$ (**6**). These were shown to reversibly dissociate in THF to generate the ionic solvates $[(\eta^3\text{-}2\text{-}RC_3H_4)Pd(NHC)(THF)]OTf$ (**7**); both **6** and **7** react irreversibly with water to give the hydrates $[(\eta^3\text{-}2\text{-}RC_3H_4)Pd(NHC)(H_2O)]OTf$ (**8**). These studies show that THF and the anionic OTf are about equally weakly nucleophilic toward Pd(II), whereas water is stronger.



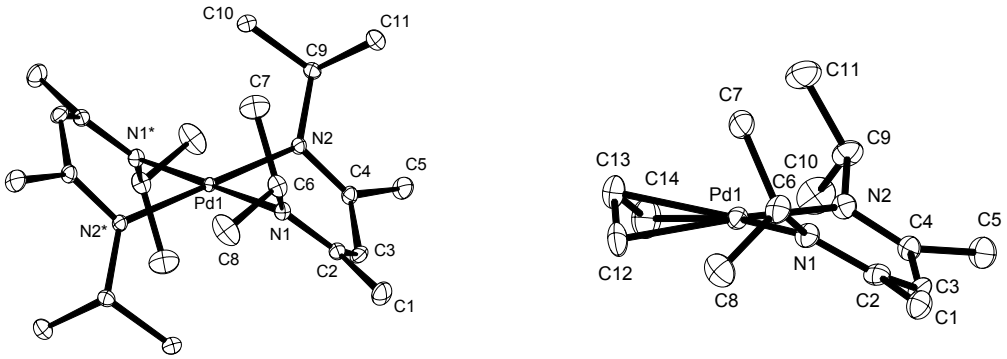

For the synthesis of complexes $(\eta^3\text{-}2\text{-}RC_3H_4)Pd(NHC)Y$ with even weaker nucleophiles Y than OTf the chlorides $(\eta^3\text{-}C_3H_5)Pd(NHC)Cl$ have been reacted with AgY (Y = $BF_4$, $PF_6$, $Al\{OC(CF_3)_3\}_4$) in $CH_2Cl_2$. For Y = $BF_4$ the undissociated adducts $(\eta^3\text{-}C_3H_5)Pd(NHC)(BF_4)$ (**9**) are isolated, whereas for Y = $PF_6$ and $Al\{OC(CF_3)_3\}_4$ the ionic $CH_2Cl_2$-solvates $[(\eta^3\text{-}C_3H_5)Pd(NHC)(CH_2Cl_2)]Y$ (**10**) separate. Examples of **9** and **10** have been characterized, inter alia, by X-ray structure analysis. When the

$CH_2Cl_2$-solvates **10** are subjected to a vacuum at ambient temperature, the $CH_2Cl_2$ evaporates and the solvent-free complexes $[(\eta^3\text{-}C_3H_5)Pd(NHC)]Y$ (Y = $PF_6$, $Al\{OC(CF_3)_3\}_4$) (**11**) remain; these await presently further characterization.



Molecular structures of $(\eta^3\text{-}C_3H_5)Pd(C\{N(^tBu)CH\}_2)(BF_4)$ (**9**) and $[(\eta^3\text{-}C_3H_5)Pd(C\{N(C_6H_3\text{-}2,6\text{-}^iPr_2)CH\}_2)(CH_2Cl_2)]PF_6$ (**10**) (cation only)

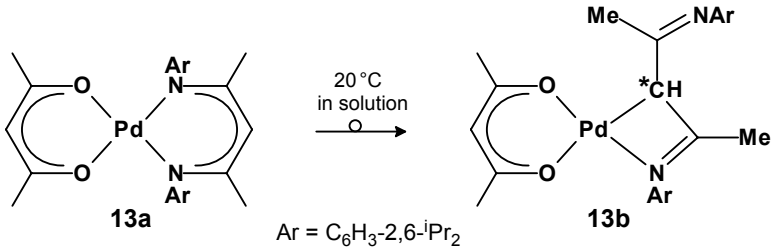
(c) We have performed a systematic study on the properties of *β*-diketiminate ligands at Pd(II), as exemplified for the *N*-isopropyl substituted $^iPr_2$-nacnac and the *N*-$C_6H_3$-2,6-$^iPr_2$ substituted $Ar_2$-nacnac ligands. $Pd(acac)_2$ reacts with Li($^iPr_2$-nacnac) via the isolatable intermediate (acac)Pd($^iPr_2$-nacnac) (**12a**) to afford the homoleptic Pd($^iPr_2$-nacnac)$_2$ (**12b**). The reaction is complicated by oxidative coupling of two $^iPr_2$-nacnac anions, concomitant with reduction of Pd, in an so far inevitable side reaction. Complex **12b** shows a rigid 2-fold envelope conformation with 12 close-packed methyl groups completely shielding the core of the complex. By reacting $\{(\eta^3\text{-}C_3H_5)Pd(\mu\text{-}Cl)\}_2$ with Li($^iPr_2$-nacnac) we have also prepared the mixed allyl/nacnac complex **12c**, likewise characterized by single crystal structure analysis.



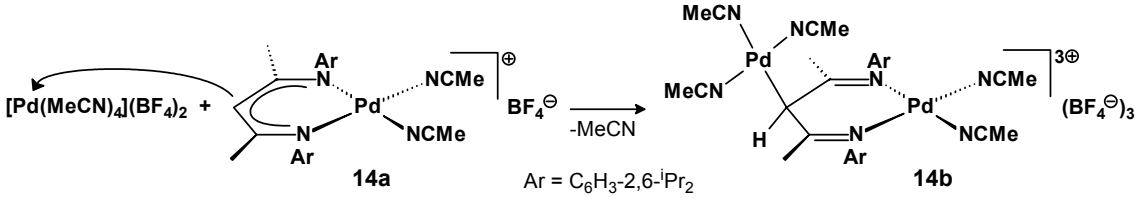

Molecular structures of Pd($^iPr_2$-nacnac)$_2$ (**12b**) and $(\eta^3\text{-}C_3H_5)Pd(^iPr_2\text{-nacnac})$ (**12c**)

The $Ar_2$-nacnac ligand is more bulky and the reaction of $Pd(acac)_2$ with Li($Ar_2$-nacnac) halts at the stage of the mixed ligand complex (acac)Pd($Ar_2$-nacnac) (**13a**). While the isolated **13a** is thermally stable at ambient temperature, it slowly isomerizes in solution

to give **13b**, bearing a novel chiral $\kappa^2$*C,N*-nacnac ligand. The latter represents a formal azaallyl, in which the electrons are localized in an enyl structure. The four-membered chelate ring is explained by a strong coordination of the central anionic carbon at Pd in the form of a Pd–C single bond and a weaker coordination of one imine nitrogen atom to complete the 4-fold coordination around Pd(II).




The retained high nucleophilicity of the central methine group in the "normal" Pd–$\kappa^2$*N,N*-nacnac complexes is also illustrated by the reaction of **14a** – obtained from $[Pd(NCMe)_4](BF_4)_2$ and $Li(Ar_2\text{-nacnac})$ – with a further 1 equiv of $[Pd(NCMe)_4](BF_4)_2$ to afford the dinuclear **14b**. In the course of this reaction the methine group displaces one acetonitrile ligand and undergoes a bridging coordination to another Pd(II) center. The electron distribution of the $\kappa^2$*N,N*-nacnac-dienyl system becomes localized in a 2,4-diimin-3-yl structure. To conclude, the $R_2$-nacnac ligands are quite versatile in their coordination modes toward the Pd(II) center. Unfortunately, the Pd(II)–$R_2$-nacnac combination, as long as acetonitrile is absent, is prone to undergo internal redox reactions resulting in decomposition, but acetonitrile significantly stabilizes the system.




**Publications resulting from this research area:** 2, 35, 379, 413, 428, 429

**External funding:** Industrial

**Cooperation:** none

### 2.2.7 Research area "Dynamically Disordered Mesophases (Plastic Crystals) of Pentacoordinate (π-Allyl)$ML_3$-type Complexes (M = Ni, Co, Rh, Ir)"

**(K.-R. Pörschke)**

**Involved:** W. Ben Mustapha, C. Creusen, R. Goddard, A. Rufinska, C. Weidenthaler

**Objective:** Following up on our discovery of the ionic $[(\pi\text{-}C_3H_5)NiL_3]Y$ (L = $P(OMe)_3$; Y = OTf (**2a**), $PF_6$ (**2b**)) complexes having plastically crystalline (PC) properties (see previous report, **2.2.6**), we have extended the range of such mesogens (a) for further anions, (b) for L = $PMe_3$, (c) for substituted π-allyl ligands, and (d) for M = Co–Ir. While plastically crystalline mesogens are still very rare in organometallic chemistry, we are now in a position to describe the properties of about 40 complexes of this type.

**Results:** We have extended the previous set of pentacoordinate, *ionic* 18e $d^8$ complexes $[(\eta^3\text{-}C_3H_5)Ni(PMe_3)_3]Y$ (**1**) and $[(\eta^3\text{-}C_3H_5)Ni\{P(OMe)_3\}_3]Y$ (**2**) (Y = OTf, $PF_6$, Br, I (**a**–**d**)) for Y = $BF_4$ (**e**), $B(C_6F_5)_4$ (**f**), $Al\{OC(CF_3)_3\}_4$ (**g**), and the "plasticizing anion" $NTf_2$ (**h**). In these complexes the occurrence of a PC mesophase results from the combined entropic contributions of the disorder in cations and anions. While $[(\eta^3\text{-allyl})NiL_3]Y$ complexes appear to withstand the formation of a mesophase for Y = halide and $BF_4$ due to the absent (halide) or low ($BF_4$) entropic contribution from the anions, the complexes $[(\eta^3\text{-}C_3H_5)Ni\{P(OMe)_3\}_3]Y$ (**2f–h**) show mesogenic properties, with **2g**,**h** displaying particulary low phase transition temperatures because of the many facile rotations of the OMe, $CF_3$, and $SO_2CF_3$ substituents in both the cation and the anions. In contrast, only one example of a $[(\eta^3\text{-}C_3H_5)Ni(PMe_3)_3]Y$ complex having PC properties has so far been realized, namely **1h** with Y = $NTf_2$. Here, the low entropic contribution from the cation is complemented by the extra high contribution from the anion. Similar results are observed for 2-methyl or syn,syn-1,3-dimethyl substitution at the allyl group. In the dynamically disordered mesophase the molecules or ions appear to rotate on their site in the lattice, giving rise to solution-type properties (e. g., in solid state NMR), although they in fact represent solids.

The results from the ionic Ni complexes directed our interest toward the known *neutral* 18e $d^8$ complexes $(\eta^3\text{-}C_3H_5)ML_3$ (M = Co (**3**, **4**), Rh (**5**, **6**), Ir (**7**, **8**); L = $PMe_3$, $P(OMe)_3$), lacking the entropic contribution of an anion. Moreover, these complexes comprise in the lattice no longer the quite strong electrostatic cation–anion interactions, but rather the much weaker van-der-Waals and dipol-dipol interactions between neutral molecules. Muetterties et al. studied the solution properties of these complexes in the 1980ies and noted already their high fluxionality, along with "waxy" solid state

properties. These were eluding the complexes from single crystal X-ray analysis at that time. We have extended the known set of complexes by the 2-methallyl derivatives, so that we were able to study the solid state phase properties of a total of 12 complexes $(\eta^3\text{-}2\text{-}RC_3H_4)ML_3$ (R = H, Me) by means of DSC (Differential Scanning Calorimetry), solid state NMR, and single crystal and powder X-ray crystallography. For the parent $(\eta^3\text{-}C_3H_5)M(PMe_3)_3$ (M = Co (**3**), Rh (**5**), Ir (**7**)) complexes we have verified the anticipated *SPY*-5 structure by single crystal X-ray analysis. All complexes form a plastically crystalline mesophase, with the phase transition temperature being highest for $(\eta^3\text{-}C_3H_5)Ir(PMe_3)_3$ (323 K) and lowest for $(\eta^3\text{-}2\text{-}MeC_3H_4)Ir\{P(OMe)_3\}_3$ (195 K), all others falling in that range. Generally, the transition temperatures are found to be (expectedly) lower for the $P(OMe)_3$ than for the $PMe_3$ complexes and (unexpectedly) much lower for the methallyl than for the parent allyl complexes. As a further noteworthy feature of these complexes, the enthalpies and entropies of the crystalline→PC phase transition as low as $\Delta H = 0.4$ kJ mol$^{-1}$ and $\Delta S = 1.5$ J mol$^{-1}$ K$^{-1}$ are unprecedented small for PC mesogens (typical values are at least 10 times as large). Also of interest, the PC Ni complexes **1**–**2** display a relatively low barrier of turnstile rotation of the three phosphorus ligands and a higher barrier for π-allyl motion (with respect to the rest of the solid). There, the additional π-allyl dynamics (Ni being now completely structural fluxional) appear to cause the occurrence of the crystalline→PC phase transition. In contrast, for the Muetterties complexes **3**–**8** in the PC phase the barrier of the π-allyl dynamics may be lower than that of the phosphorus turnstile rotation; that is, the phosphorus ligand dynamics may already be "frozen out", while the allyl group is still in motion (apparently, π-allyl motion necessarily accompanies the formation of a PC phase). Here, structurally rigid *SPY*-5 molecules appear to rotate on their sites in the lattice.

**Publication resulting from this research area:** 359

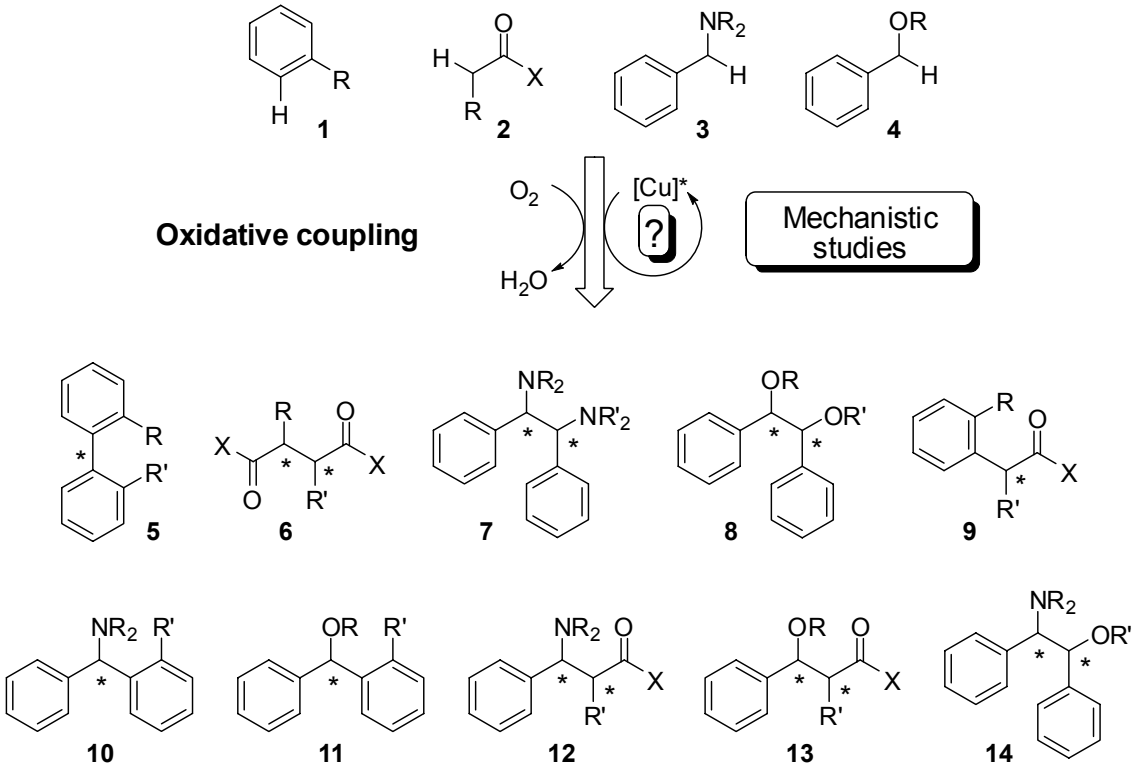
**External funding:** DAAD

**Cooperations:** M. Bühl (Mülheim/Ruhr, DE)

### 2.2.8 Research Area „Copper-Catalyzed Asymmetric Oxidative Coupling Reactions for the Formation of Carbon-Carbon Bonds" (M. Klußmann)

**Involved:** E. Böß, A. Sud, D. Sureshkumar

**Objective:** Oxidative coupling allows for the direct CC-coupling of two fragments with cleavage of a carbon-hydrogen (CH) bond each, resulting in a net oxidation of the fragments. The reaction can be catalyzed by metal compounds with the use of atmospheric oxygen with water as the side product. Examples for this type of reaction are long known, yet many of these still suffer from low activity or selectivity or are performed with stoichiometric amounts of metal compounds as oxidant. Furthermore, there is to date no satisfying understanding of the reaction mechanism(s) and contradictory models occasionally serve as the basis for reaction development.
This gap in understanding is planned to be filled by the present research project. Therefore, mechanistic studies will go hand in hand with reaction development. The substrate scope for oxidative coupling reactions is large, e.g. **1**-**4**, and as both homo- and heterocoupling is possible, a large variety of products **5**-**14** is possible, as shown below.




Eventually, this project will lead to the development of catalytic systems to couple a whole variety of substrates in new ways to a plethora of potentially chiral products,

many of which still pose a challenge today. Additionally, these reactions will satisfy modern requirements as they will only utilize catalytic amounts of a relatively cheap metal compound (Cu), will not require preactivated substrates (simply CH-bonds next to a directing group), use an environmentally benign oxidation agent ($O_2$) and will be basically waste-free (water as the only by-product).

**Publications resulting from this research area:** none

**External funding:** none

**Cooperation**: none

### 2.2.9 Research Area „Asymmetric Amplification by Phase Behaviour with Potential Implications for the Origin of Life" (M. Klußmann)

**Involved:** E. Böß, A. Sud

**Objective:** The origin of life is one of the most intriguing puzzles in science, with the evolution of biological homochirality from a presumably racemic primordial earth being a particularly puzzling piece for chemists dealing with chirality. Amongst several different models, phase behaviour has been evoked as a way of amplifying small imbalances in enantiomeric composition to high excesses of one enantiomer. A striking example is the amino acid serine which in solid-solution equilibrium can attain nearly enantiopure solutions. But even for other compounds such strong amplification can be possible if the crystal structure of the solid phase is accordingly altered.
Based on these previous results, I plan to investigate the phase behaviour of one amino acid in the presence of an additional cocrystalizing substance. Any change in crystal structure will lead to a change of solution behaviour and could lead to stronger chiral amplification. Ultimately, more complex systems will be investigated, as aqueous solutions containing several amino acids and other compounds are a much more likely scenario for the prebiotic soup than just a single substance. An amplified solution ee will then provide the basis for chirality transfer to new biologically important products via solution phase reactions. Investigations are planned on the formation of peptides which could themselves be used as catalysts for asymmetric carbohydrate synthesis. Thus, a model might be developed of how homochirality in biological building blocks could have been achieved by an interplay of "prebiotic crystal engineering" and catalysis.
These studies on complex solid-solution systems will have major implications beyond the field of prebiotic chemistry; the study of cocrystals and their phase behaviour, for example, will contribute to the growing field of crystal engineering and holds importance for the pharmaceutical industry.

**Publication resulting from this research area:** 411, 412, 467

**External funding:** none

**Cooperation**: D.G. Blackmond (Imperial College, London, UK)