Highlights from OMCOS 18

Andrea Ambrosi
Denmark group meeting
July 28, 2015

OMCOS

- Conceived by John Stille and Giorgio Modena in 1979
- The first symposium took place at Colorado State University (Fort Collins) in 1981 (key speakers: Posner, Kumada, Noyori, Heck, Tsuji, Larock, Negishi, Semmelhack, Trost)
<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Event Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>Seoul</td>
<td>Chairs: Sukbok Chang, Chulbom Lee</td>
</tr>
<tr>
<td>2015</td>
<td>Sitges, Barcelona, Spain</td>
<td>June 28 – July 2</td>
</tr>
<tr>
<td>2013</td>
<td>Ft. Collins</td>
<td>July 28 - August 1</td>
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<tr>
<td>2011</td>
<td>Shanghai</td>
<td>July 24 - 28</td>
</tr>
<tr>
<td>2009</td>
<td>Glasgow</td>
<td>July 26 - 30</td>
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<tr>
<td>2007</td>
<td>Nara</td>
<td>August 2 - 6</td>
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<td>2005</td>
<td>Geneva</td>
<td>July 17 - 21</td>
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<td>2003</td>
<td>Toronto</td>
<td>July 6 - 10</td>
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<td>2001</td>
<td>Taipei</td>
<td>July 22 - 26</td>
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<td>1999</td>
<td>Versailles</td>
<td>July 18 - 22</td>
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<td>1997</td>
<td>Goettingen</td>
<td>July 20 - 25</td>
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<tr>
<td>1995</td>
<td>Santa Barbara, California</td>
<td>August 6 - 10</td>
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<tr>
<td>1993</td>
<td>Kobe</td>
<td>September 19 - 23</td>
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<tr>
<td>1991</td>
<td>Utrecht</td>
<td>August 25 - 29</td>
</tr>
<tr>
<td>1989</td>
<td>Florence</td>
<td>October 1 - 6</td>
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<tr>
<td>1987</td>
<td>Vancouver</td>
<td>July 26 - 30</td>
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<tr>
<td>1985</td>
<td>Kyoto</td>
<td>July 11 - 15</td>
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<tr>
<td>1983</td>
<td>Dijon</td>
<td>August 28 - September 1</td>
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<tr>
<td>1981</td>
<td>Fort Collins, Colorado</td>
<td>August 2 - 6</td>
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</table>

**Sitges, Spain**

![Sitges Map](image)
Sitges, Spain

Format

- Single venue
- ca. 900 attendees
- 23 invited lectures/plenary lectures (30-50 min)
- 28 oral communications (15 min)
- > 600 posters (2 sessions)
**Reductive Acyl-Benzyl Cross-Coupling**

This work:

\[
\text{RCl} + \text{ArCl} \rightarrow \text{RC} = \text{Ar}
\]

- direct ketone formation
- no pregeneration of organometallic reagents
- no stoichiometric chiral auxiliaries
- high functional group tolerance
- no epimerization of tertiary center


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**Sarah Reisman**

**NiCl₂(dme) (10 mol %)**

\[
\begin{align*}
\text{RCOCl} + \text{ArCl} & \rightarrow \text{RCOCl} + \text{ArCl} \\
\text{NiCl}_2(\text{dme}) (10 \text{ mol} \%) & \rightarrow \text{NiCl}_2(\text{dme}) (10 \text{ mol} \%)
\end{align*}
\]

Mn⁰, DMBA

30% v/v DMA/THF

3Å MS, 20 °C

Reductive Vinyl-Benzyl Cross-Coupling

\[ R-\text{Ar} + \text{Ph-CHCl} \xrightarrow{\text{NiCl}_2(dme), \text{L}6} \text{R-CHPh} \]

1 (1.0 equiv) 2a (1.0 equiv)

80% yield, 91% ee* 82% yield, 92% ee 55% yield, 96% ee
72% yield, 94% ee 56% yield, 94% ee
77% yield, 94% ee* 40% yield, 90% ee

Sarah Reisman

Reductive Aryl-Nitrile Cross-Coupling

\[
\text{I} + \text{R-CN} \xrightarrow{\text{NiCl}_2(\text{dme}) \text{Mn}} \text{R-CN}
\]

aromatic/heteroaromatic

Troels Skrydstrup

Ex Situ Generation of Stoichiometric CO

\[
Pd(dbu)_2 (5 \text{ mol\%}) + \text{DIPEA (1 equiv)} \xrightarrow{\text{Dioxane, 80 °C}} \text{DIPEA-HCl} + \text{CO(g)}
\]

Troels Skrydstrup

**Chemical Reaction**

1. **9-Fluorenone**
   - Treatment with MeMgl to obtain 91% yield.
   - Recrystallization to achieve purity.

2. **9-Methyl-9H-fluorenne**
   - Reaction with n-BuLi, THF, -78 °C, 1. CO₂, excess.
   - Yield: 91%.
   - Reaction with (COCl)₂ (3 equiv) in DMF (cat).
   - Yield: Quantitative.

3. **Pd(dba)₂ (5 mol%)**
   - Reaction with P(Ph)₂(Bu)₃ (5 mol%) and DIPEA (1.5 equiv).
   - Reaction in Dioxane, 80 °C.
   - CO₂(g) or [¹³C]CO₂(g).

4. **9-Methylene-fluorene**
   - Reaction with Pd/C, H₂.
   - Yield: 58%.

**Table**

<table>
<thead>
<tr>
<th>Entry</th>
<th>(Het)Ar-X</th>
<th>Product</th>
<th>25°</th>
<th>*25°</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>PET Tracer for melanoma (27)</td>
<td>86%</td>
<td>87%</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>H₂ Receptor antagonist (28)</td>
<td>83%</td>
<td>90%</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Ispride (29)</td>
<td>94%</td>
<td>89%</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>CX-546 (30)</td>
<td>83%</td>
<td>95%</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Metaclopamide (31)</td>
<td>63%</td>
<td>62%</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Brexpiprazine (32)</td>
<td>65%</td>
<td>66%</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>Cor of PARP1 Inhibitors (33)</td>
<td>84%</td>
<td>75%</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>Losartan precursor (34)</td>
<td>79%</td>
<td>89%</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>Butoxycauline (35)</td>
<td>89%</td>
<td>91%</td>
</tr>
</tbody>
</table>

Troels Skrydstrup

Vladimir Gevorgyan

Palladium-Catalyzed Silanol-Directed C-H activation

- Alkenylation

- Carboxylation


Conversion of 1-alkenes into 1,4-diols

Cathleen Crudden

Cross Coupling Reactions of Chiral Secondary Organoboronic Esters


Hydrogenations with Mesoionic Carbene-Stabilized Borenium Catalysts

Helmut Schwarz

- Worked as a laboratory technician in chemical industry (Dynamit Nobel AG)
- Failed to pursue a professional career as a soccer player
- Completed his Ph.D. in 1972 at Technische Universität Berlin (TUB) under the supervision of the natural product chemist Ferdinand Bohlmann
- Spent some time abroad (ETH Zürich, Cambridge University, and MIT)
- In 1978 he returned to his alma mater to join the Institute of Chemistry
- Has occupied visiting and academic positions at 15 research institutions worldwide
- Published close to 1000 peer-reviewed articles
- Delivered more than 900 invited or name lectures
- Since January 2008 Dr. Schwarz has served as President of the Alexander von Humboldt-Stiftung
Franziska Schoenebeck

Reductive Elimination of ArCF₃:
the predictive power of computational analysis


Franziska Schoenebeck

Computationally Designed Complex:

Predicted Barrier: \( \Delta E^\ddagger = 24.8 \text{ kcal mol}^{-1} \)

Franziska Schoenebeck

Combining the Reactivity Properties of PCy₃ and PtBu₃ into a Single Ligand, P(iPr)(tBu)₂

Increasing Steric Effects

Reactivity:
PdL₄:  ❌  ✔  ✔  ✔
PdL₃:  ✔  ✔  ✔  ❌
L-Pd(III)-Pd(II)-L:  ❌  ✔  ✔  ✔

Ligand controls Pd-palp stability:

consistent with [Pt(Ph₂)] as active species
consistent with [PtL₂] as active species


Carsten Strohmann

Insights into the Metalation by Schlosser’s Base

Electrophile | E   | yield |
-------------|------|-------|
6a           | BuCl | 92%   |
6b           | Me₃SiCl | 84%   |
6c           | Ph₂MeSiCl | 60%   |
6d           | Ph₂CO  | 74%   |
6e           | C₂H₁₀CO | 84%   |

Deprotonation of benzene:

\[ [(\text{PhK})_4(\text{PhLi})(t\text{BuOLi})(\text{THF})_6(\text{C}_6\text{H}_6)_2] \]

Deprotonation of toluene:

\[ [(\text{BnK})_3(\text{THF})_4] \]


Jan Streuff

Low-Valent Transition Metal Catalyzed Reductive Umpolung Reactions

### Cross-selective acyloin reaction

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Products</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a + [Cp₂TiCl₃] (10 mol%) + Zn (2.0 equiv)</td>
<td>3a-p</td>
<td>THF, 35 °C</td>
</tr>
<tr>
<td>1a + N,N-Dimethylcarbamoyl chloride</td>
<td>3q</td>
<td>73%</td>
</tr>
</tbody>
</table>

Naoki Ishida

Light and C-C activation: cyclophanes


Naoki Ishida

Naoki Ishida

Light and C-C activation: hydroxypyperidines


Naoki Ishida

Synthesis and reactivity of allylboronic acids

Table 1: Synthesis and isolation of allylboronic acids.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Cat. (mol%)</th>
<th>Solvent (molarity)</th>
<th>t [h]</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>2a (0.5)</td>
<td>MeOH (1.0)</td>
<td>18</td>
<td>Pinacol</td>
<td>61*</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>2a (0.5)</td>
<td>MeOH (1.0)</td>
<td>0.2</td>
<td>BrPinacol</td>
<td>80*</td>
</tr>
<tr>
<td>3</td>
<td>Br</td>
<td>2a (0.2)</td>
<td>DMSO</td>
<td>2</td>
<td>BrPinacol</td>
<td>71*</td>
</tr>
<tr>
<td>4</td>
<td>OH</td>
<td>2a (0.2)</td>
<td>DMSO/MeOH 3:2 (1.0)</td>
<td>14</td>
<td>BrPinacol</td>
<td>55*</td>
</tr>
<tr>
<td>5</td>
<td>Ph</td>
<td>2a (2.0)</td>
<td>DMSO/MeOH 4:1 (1.0)</td>
<td>13</td>
<td>BrPinacol</td>
<td>71*</td>
</tr>
</tbody>
</table>

Table 2: Reaction of allylboronic acids with ketones.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Boronic acid</th>
<th>Ketone</th>
<th>Solvent</th>
<th>t [h]</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4a</td>
<td>5a</td>
<td>THF</td>
<td>1</td>
<td>6a</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>4a</td>
<td>5b</td>
<td>THF</td>
<td>24</td>
<td>6b</td>
<td>89</td>
</tr>
<tr>
<td>3</td>
<td>4a</td>
<td>6a</td>
<td>DMSO</td>
<td>14</td>
<td>6a</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>4a</td>
<td>5d</td>
<td>THF</td>
<td>22</td>
<td>6d</td>
<td>90</td>
</tr>
</tbody>
</table>


Table 3: Reaction of imines with boronic acids.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Boronic acid</th>
<th>Imine</th>
<th>Time (h)</th>
<th>Product</th>
<th>Yield [%]</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>1a</td>
<td>1</td>
<td>3a</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>2a</td>
<td>1b</td>
<td>3</td>
<td>3b</td>
<td>84*</td>
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<tr>
<td>9</td>
<td>2a</td>
<td>1f</td>
<td>1</td>
<td>3f</td>
<td>93</td>
</tr>
<tr>
<td>10</td>
<td>2a</td>
<td>1g</td>
<td>24</td>
<td>3j</td>
<td>65</td>
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</tbody>
</table>

Fig. 2. Reaction profile for the allylboration of 1a in the presence of allylboroxine 2a. The ΔG values are given in kcal mol⁻¹.

Fig. 3. Allylboration of 1a with cinnamyl boronic acid 2a. The ΔG values are given in kcal mol⁻¹.