

## Conferencia: Noncovalent substrate-directing effects in enantioselective Heck reactions. Recent applications in organic synthesis

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# NONCOVALENT SUBSTRATE-DIRECTING EFFECTS IN ENANTIOSELECTIVE HECK REACTIONS. RECENT APPLICATIONS IN ORGANIC SYNTHESIS

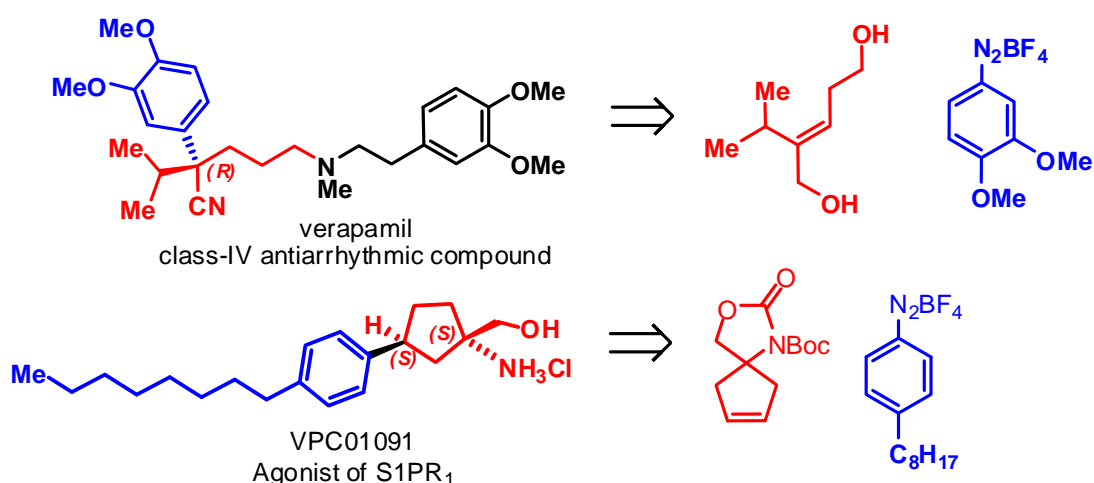
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The enantioselective Heck arylation of olefins has been the subject of intense studies in the last decades due to its outstanding potential to generate new drugs, functional materials, fragrances, and other important compounds.

In this context, the palladium catalyzed coupling of arenediazonium salts to olefins (Heck-Matsuda reaction)<sup>1</sup> represents a robust and reliable method to access complex intermediates for the synthesis of complex functional and bioactive molecules. The Heck-Matsuda arylations have many advantages over the conventional Heck protocols. We recently reported that non-covalent effects can strongly influence the outcome of these reactions directing the diastereoselectivity and enantioselectivity of these reactions in a pseudo-intramolecular process.<sup>2</sup> We have also discovered that these effects are not restricted to the Heck-Matsuda, but are also present in other Heck reactions, such as the oxidative Heck reactions.

This lecture will present recent results from my laboratory to perform effective asymmetric Heck-Matsuda reactions employing chiral *N,N*-ligands, to synthesize challenging chiral tetrasubstituted tertiary centers, and quaternary spiro stereogenic centers, together with applications in the enantioselective total synthesis of pharmacologically active compounds, such as verapamil and VPC01091 – a clinical candidate for the treatment of multiple sclerosis.<sup>2c,3</sup>



1. Review: Taylor, J. G.; Moro, A. V.; Correia, C. R. D. *Eur. J. Org. Chem.* **2011**, 1403–1428.
2. (a) Kattela, S.; Heerdt, G.; Correia, C. R. D. *Adv. Synth. Cat.* **2017**, 359, 260–267; (b) de Oliveira, J. S.; Angnes, R. A.; Menezes, V. H. S.; Servilha, B.; Adeel, M.; Braga, A.; Aponick, A.; Correia, C. R. D. *J. Org. Chem.* **2016**, 81, 2010–2018; (c) Correia, C. R. D.; Azambuja, F.; Carmona, R. C.; Chorro, T.; Heerdt, G. *Chemistry – A European Journal*, **2016**, 22, 11205–11209. (d) Oliveira, C. C.; Pfaltz, A.; Correia, C. R. D. *Chem. Angew. Chem. Int. Ed.* **2015**, 54, 14036–14039.
3. (a) Khan, I. U.; Kattela, S.; Hassan, A.; Correia, C. R. D. *Org. Biomol. Chem.* **2016**, 14, 9476–9480, (b) Carmona, R. C.; Correia, C. R. D. *Adv. Synth. Cat.* **2015**, 357, 2639–2643.

**Name: CARLOS ROQUE DUARTE CORREIA**

**1. Present Position:** Full Professor of Chemistry; State University of Campinas (Unicamp), since 2009

**Previous Positions:** Associate Professor of Chemistry, Level 5 – Unicamp (2001-2009)  
Associate Professor of Chemistry, Level 4 – Unicamp (1993-2001)  
Associate Professor – Federal University of Rio de Janeiro (1990-1993)  
Visiting Assistant Professor – Federal University of Rio de Janeiro (1987-1990)

## 2. Education/Training

**Ph.D.** - Chemistry – Stanford University, EUA (1986), Chemistry, adviser: Prof. Paul Anthony Wender

**M.Sc.** - Chemistry of Natural Products (1980)

**B.S.** - Federal University of Rio de Janeiro, Brazil, Pharmacy, (1976)

## 3. Appointments

**2014-2016:** Associate Head – Chemistry Institute Research Committee

**2013-2015 and 2008-2009:** Vice-Head of the Organic Chemistry Department

**2010 – 2012 and 2005-2006:** Coordinator of Unicamp School of Pharmacy

**2009-2010:** Associate Director of the Chemistry Institute, Unicamp

**2001-2003:** General Secretary of the “10th Brazilian Meeting on Organic Synthesis” held in August 24-28, 2003, São Pedro, São Paulo, Brazil.

**1999-2006:** Vice-Head of the Graduate Studies Committee, Chemistry Institute, Unicamp

**1998-1999:** Head of the Graduate Studies Committee, Chemistry Institute, Unicamp

**1994-1996:** Treasure for the Brazilian Chemical Society

## 4. Publications

### 4.1. Selected publications in the last 5 years (out of a total of 113 publications):

1. Shivashankar Kattela, Gabriel Heerdt, and Carlos Roque Duarte Correia **"Non-Covalent Carbonyl-Directed Heck-Matsuda Desymmetrizations: Synthesis of Cyclopentene-fused Spirooxindoles, Spirolactones, and Spirolactams"**. *Adv. Synth. Cat.* **2017**, 359, 260–267.
2. de Oliveira Silva, Juliana; Angnes, Ricardo; Menezes da Silva, Vitor H.; Servilha, Bruno; Adeel, Muhammad; Braga, Ataulpa; Aponick, Aaron; Correia, Carlos Roque , **"Intermolecular Noncovalent Hydroxy-Directed Enantioselective Heck Desymmetrization of Cyclopentenol: Computationally-driven Synthesis of Highly Functionalized *cis*-4-Aryl-Cyclopentenol Scaffolds"** *J. Org. Chem.* **2016**, 81, 2010-2018.
3. Ismat Ullah Khan, Shivashankar Kattela, Abbas Hassan and Carlos Roque Duarte Correia\*, **Enantioselective Total Synthesis of the Highly Selective Sphingosine-1-Receptor VPC01091 by Heck Desymmetrization of a Non-Activated Cyclopentene-Fused Spiro-Pyrrolidinone**, *Org. Biomol. Chem.*, **2016**, 14, 9476–9480. Paper highlighted in Synfacts: *Synfacts* **2017**, 13(01), 0016;
4. Caio C. Oliveira, Andreas Pfaltz, and Carlos Roque Duarte Correia **"Quaternary Stereogenic Centers through Enantioselective Heck Arylation of Acyclic Olefins with Aryldiazonium Salts: Application in a Concise Synthesis of (*R*)-Verapamil"** *Angew. Chem. Int. Ed.* **2015**, 54, 14036 –14039. DOI: 10.1002/anie.201507927. Paper highlighted in Synfacts (*Synfacts* **2016**, 12(2), 0109;
5. (Review) Ricardo A. Angnes, Zhou Li, Carlos Roque D. Correia, and Gerald B. Hammond **"Recent synthetic additions to the visible light photoredox catalysis toolbox"** *Organic & Biomolecular Chemistry*, **2015**, 13, 9152 – 9167.
6. Rafaela C. Carmona and Carlos Roque D. Correia, **"Stereoselective synthesis of 3-hydroxy-4-arylcyclopentanones and 4-arylcyclopentenones through a Heck-Matsuda desymmetrization of *meso cis*-4-cyclopentene-1,3-diol"**, *Adv. Synth. Catal.* **2015**, 357, 2639-2643.

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7. Ricardo A. Angnes, Juliana M. Oliveira, Caio C. Oliveira, Nelson C. Martins and Carlos Roque D. Correia, **Stereoselective Synthesis of Aryl Cyclopentene Scaffolds by Heck-Matsuda Desymmetrization of 3-Cyclopentenol**, *Chemistry – A European Journal* **2014**, *20*, (41), 13117–13121. **Highlighted in Synfacts** **2014**, *10* (11), 1168.
  8. Correia, Carlos Roque; Oliveira, Caio; Marques, Marcelo; Godoi, Marla; Regiani, Thais; Santos, Vanessa; Santos, Emerson; Eberlin, Marcos; Sá, Marcus **"Chemo-, Regio- and Stereoselective Heck Arylation of Allylmalonates: Mechanistic Insights by ESI-MS and Synthetic Application toward 5-Arylmethyl- $\gamma$ -lactones"** *Org. Lett.* **2014**, *16*, 5180–5183.
  9. Book Chapter: **"Substrate-Directed Heck-Matsuda Arylations. From Curiosity to a Valuable Synthetic Tool"**, Oliveira, C. C.; Correia, C. R. D. In *Strategies and Tactics in Organic Synthesis*; Michael Harmata, Ed.; Academic Press, **2014**; Volume 10, pp. 1–32.
  10. Patrícia Prediger, Allan Ribeiro da Silva, and Carlos Roque Duarte Correia. **"Construction of 3-Arylpropylamines by Heck arylations. Total Synthesis of Cinacalcet Hydrochloride, Alverine, and Tolpropamine"** *Tetrahedron*, **2014**, *70*, 3333–3341. Brazilian Meeting on Organic Synthesis Commemorative Issue.
  11. Caio C. Oliveira, Ricardo A. Angnes and Carlos Roque D. Correia **"Intermolecular Enantioselective Heck-Matsuda Arylations of Acyclic Olefins. Application to the Synthesis of  $\beta$ -Aryl- $\gamma$ -Lactones and  $\beta$ -Aryl Aldehydes"** *J. Org. Chem.* **2013**, *78*, 4373–4385
  12. Angelo H. L. Machado, Humberto M. S. Milagre, Livia S. Eberlin, Adão A. Sabino, Carlos Roque D. Correia and Marcos N. Eberlin **"Dbu-free" palladium intermediates of the Heck–Matsuda reaction"** *Org. Biomol. Chem.* **2013**, *11*, 3277–3281. **Inside cover**
  13. Carlos Roque D. Correia, Caio C. Oliveira, Ailton G. Salles Jr., Emerson A.F. Santos, **The first examples of the enantioselective Heck–Matsuda reaction: arylation of unactivated cyclic olefins using chiral bisoxazolines**, *Tetrahedron Lett.* **2012**, *53*, 3325–3328. *First report for such reaction.*
  14. Caio C. Oliveira, Emerson A. F. dos Santos, Julia H. Bormio Nunes and Carlos Roque D. Correia; **Stereoselective Arylation of Substituted Cyclopentenones by Substrate-Directable Heck-Matsuda reactions. A Concise Total Synthesis of the Sphingosine 1-Phosphate Receptor (S1P1) agonist VPC01091.** *Journal of Organic Chemistry*, **2012**, *77*, 8182–8190
  15. Jason G. Taylor, Angélica V. Moro, Carlos Roque D. Correia **"Evolution and Synthetic Applications of the Heck–Matsuda Reaction: The Return of Arenediazonium Salts to Prominence.** *Eur. J. Org. Chem.* **2011**, 1403–1428. **Among the 25 most cited review articles in this journal in 2012.**

#### 4.2. Patents (out of 8):

16. **International Patent: "Xilitolol Esteres and Ethers Applied as Alternative Emulsifiers, Solvents, Co-emulsifiers and Preservative Systems for Pharmaceutical and Cosmetic Products"**. PCT/IB200/054321, October 28, 2008; International Bureau of the World Intellectual Property Organization: P-791, authors: Maria Del Carmen Velazquez Pereda; Marcio Antonio Polezel, Gustavo de Campos Dieamant; Cecília Nogueira, Carlos Roque Duarte Correia; Lilian Mussi; Marcos Roberto Rossan; Nilton Soares Camilo.

17. **International Patent:** “**Topical Composition Comprising Phosphates, Phosphonates, Phosphites and Phosphoramidates for Topical Application to Hair and/or Skin**”. PCT/IB2009/054883, November 03, 2009; International Bureau of the World Intellectual Property Organization: P-811, authors: Maria Del Carmen Velazquez Pereda; Marcio Antonio Polezel, Gustavo de Campos Dieamant; Cecília Nogueira, Carlos Roque Duarte Correia; Nilton Soares Camillo; Jessica Eleonora Pedroso Sanches Silveira.

**5. Awards:**

- **CAPES, “Best PhD Thesis Award 2016: Earth Sciences”**, a national contest for the best PhD. dissertation in Chemistry in 2015 in Brazil, PhD student: Caio Costa Oliveira.
- **The “Zeferino Vaz Excellence Award” (2013)**, UNICAMP, for research in the Chemical Sciences
- **Nicola Petragani Award (2012)**, for the best work/study presented at the 35th Annual Meeting of the Brazilian Chemical Society.
- **CAPES, Honorary Mention in the “Best PhD Thesis Award 2012”**, for the PhD. dissertation in Chemistry in 2011, graduate student: Angélica Venturi Moro.
- **“Non-Tenured Faculty Awards” 3M Company (2000)**, “2nd University Day”, Sumaré, São Paulo. For chemical research with potential technological applications

**6. Quantitative indicators:**

- 1) Books: 1
- 2) Publications: 113
- 3) Plenary Lectures, seminars, talks: 108
- 4) Master thesis supervised: 25
- 5) Ph.D. dissertations supervised: 31
- 6) Post Doctors supervised: 21
- 7) Supervision of undergraduates w/ research fellowship: 35
- 8) Posters (national and international events, congresses): more than 400

**7. Link web MyResearcherID and/or MyCitation (Google Scholar):**

<http://www.researcherid.com/rid/C-2273-2012>

**8. Other relevant information:**

- **Level 1A scientist of the Brazilian National Research Council**
- **Fellow of the Royal Society of Chemistry**
- **Member of the Brazilian National Research Council, Chemistry Committee**
- **Editor for Latina America** of the journal **Letters in Organic Chemistry**, Betham Science (2015-2017). Member of the advisory board of **Chemical Data Collections** (RSC); and **Organocatalysis** (Betham Science).
- **Scientific Adviser**, International Foundation for Science (IFS, Sweden), since 1994.
- **Commissions/meeting organizations: on several occasions for the Brazilian Meeting on Organic Synthesis (general secretary for the 10<sup>th</sup> Edition, in 2003), Brazil-Spain Workshop in Organic Chemistry since its first edition (5<sup>th</sup> edition in 2016).**
- **H-index = 30** (Web of Science, Correia, CRD, December/2016)