

## FABIO PRATI

### *Curriculum Vitae*

**Fabio Prati** is full professor of Organic Chemistry at the University of Modena and Reggio Emilia (UNIMORE, <https://www.unimore.it> ; <https://international.unimore.it> ), Department of Life Sciences.

#### **Personal information**

Researcher unique Identifier(s): ORCID: 0000-0002-0650-9540; SCOPUS ID: 7006548521

Date of birth: May 18, 1960

Nationality: Italian

URL for web site: <http://personale.unimore.it/rubrica/dettaglio/fprati>

#### **Education and Positions**

1984 – University of Modena, Degree in Chemistry *cum laude*

1985-1986: National Civil Service – Caritas Italiana

1986-1989: PhD in Chemical Sciences, University of Parma-Modena-Ferrara

1989-1992: Teacher of Chemistry – High Schools

1992-2000: Researcher, permanent position - UNIMORE, Department of Chemistry

2000-2012: Associated professor - UNIMORE, Faculty of Pharmacy

2013 - now: Professor of Organic Chemistry - UNIMORE, Department of Life Sciences

#### **Academic responsibilities.**

2013-2014 - Scientific Director of the Scientific Library - UNIMORE

2014: Director of the Department of Life Sciences UNIMORE

2016-2021: Dean of the degree course (five years) of Pharmaceutical Chemistry and Technology

2019-2021: Member of the Cabinet Council - Department of Life Sciences UNIMORE

2021 - now: Quality Assurance Manager – Department of Life Sciences UNIMORE

#### **Teaching activity.**

His teaching activity has been mainly delivered within the degree course of Chemistry (Laboratory of Organic Chemistry 2, 100 hours, from 1996 to 2002), the degree course of Pharmacy (Organic Chemistry, 80 hours, from 1998 to 2003), and Pharmaceutical Chemistry and Technology (Organic Chemistry 1 and Organic Chemistry 2, 72 hours each, from 2003 until now). He was/is member of the following Doctoral Schools: Doctoral School of Chemistry (from 1996 to 2004), Doctoral School of Science and Technology of Health Products (from 2005 to 2012), and Doctoral School of Clinical and Experimental Medicine (from 2013 until now).

#### **Supervision of graduate students and postdoctoral fellows.**

Prof Prati has been supervisor of 11 PhD students; he has been tutoring 9 postdoctoral fellows for collectively 15 years.

## Contributions to Science

At the beginning of his research, he has been interested in enzymatic catalysis applied to organic synthesis, aiming to enantioselective synthesis of biologically active heterocycles or their precursors. In this context he was able to obtain by hydrolase-catalyzed reactions enantiomerically pure form of aziridines bearing stereogenic nitrogen as unique asymmetric center; he also developed a method for the enantioselective synthesis of both enantiomers of 3-hydroxyesters by baker's yeast by selective inhibition of the pro-*R* and pro-*S* dehydrogenases. In collaboration with prof. H. Alper (Ottawa University - Canada) he was then interested in homogeneous catalysis, exploring the carbonylative ring expansion of aziridines to beta-lactam, where he highlighted scope and limitation of this method.

- Bucciarelli Maria; Forni Arrigo; Moretti Irene; Prati Fabio. *Enzymatic resolution of chiral N-alkyloxaziridine-3,3-dicarboxylic esters*. Chemical Communications, 1988, 1614-15
- Bucciarelli Maria; Forni Arrigo; Moretti Irene; Prati Fabio; Torre Giovanni. *Enzymatic resolution of aziridine carboxylates*. Tetrahedron: Asymmetry, 1993, 4, 903-6.
- Antolini L.; Bucciarelli M.; Caselli E.; Davoli P.; Forni A.; Moretti I.; Prati F.; Torre G. *Stereoselective Synthesis of Erithro  $\beta$ -Substituted Aspartates*. Journal of Organic Chemistry, 1997, 62, 8784-8789
- Davoli Paolo; Moretti Irene; Prati Fabio; Alper Howard. *Carbonylation of Silylated Hydroxymethyl Aziridines to  $\beta$ -Lactams*. Journal of Organic Chemistry 1999, 64, 518-521.
- Davoli Paolo; Forni Arrigo; Moretti Irene; Prati Fabio\*; Torre Giovanni. *On the effect of ring substituents in the carbonylation of aziridines*. Tetrahedron 2001, 57, 1801-1812.
- Attanasi Orazio A.; Davoli Paolo; Favi Gianfranco; Filippone Paolino; Forni Arrigo; Moscatelli Giada; Prati Fabio. *Azavinyl Azomethine Ylides from Thermal Ring Opening of  $\alpha$ -Aziridinohydrazones: Unprecedented 1,5-Electrocyclization to Imidazoles*. Organic Letters, 2007, 9, 3461-3464.

By combining enzymatic resolution of suitable functionalized aziridine(s) and regioselective carbonylative ring expansion, he succeeded in the total synthesis of the carbapenem antibiotic PS-5. Along this line of homogeneous catalysis, he faced the total enantioselective synthesis fungi metabolites by ring-closing metathesis, identifying new stereoselective methodologies by means of boronic esters.

- C Boga, S Drioli, C Forzato, G Micheletti, P Nitti\*, G Pitacco, F Prati. *An easy route to enantiomerically pure 7- and 8-HSA by olefin metathesis-based approach*. SynLett – 2016, 1354-1358.
- Davoli Paolo; Prati Fabio. *A novel approach to a precursor of the carbapenem antibiotic PS-5 via aziridine stereospecific carbonylation*. Heterocycles, 2000, 53, 2379-2389.
- Caselli Emilia, Danieli Chiara, Morandi Stefania, Bonfiglio Beatrice, Forni Arrigo, Prati Fabio\*. *(S)-(+)-N-Acetylphenylglycineboronic acid: A Chiral Derivatizing Agent for ee Determination of 1,2-diols*. Organic Letters, 2003, 5, 4863-4866.
- Davoli Paolo, Spaggiari Alberto, Castagnetti Luca, Prati Fabio\*. *Total Synthesis of (–)-Microcarpalide, a Novel Microfilament Disrupting Agent*. Organic and Biomolecular Chemistry, 2004, 2, 38-47.
- S. Morandi, F. Pellati, C. Ori, B. Adinolfi, P. Nieri, S. Benvenuti, F. Prati\*. *Isolation, structure elucidation and total synthesis of a cytotoxic dienone from Echinacea pallida*. Organic & Biomolecular Chemistry, 2008, 6, 4333 – 4339.

In close collaboration with molecular biologists (prof. Brian Shoichet, University of California San Francisco), crystallographers and microbiologists (prof. R Bonomo, Case Western Reserve University – Cleveland), he was fostered to develop the synthesis of acylaminoboronic acids for the inhibition of beta-lactamases, bacterial enzymes responsible of the growing antibacterial resistance. In this field he rationally designed and synthesized enantiomerically pure boronic acids as selective and potent inhibitors of the targeted enzymes, obtaining several nM inhibitors of beta-lactamases, capable of restoring *in vitro* the antibacterial activity of beta-lactam antibiotics.

- Chen Yu; Minasov George; Roth Tomer A.; Prati Fabio; Shoichet Brian K.\* *The deacylation mechanism of AmpC  $\beta$ -lactamase at ultrahigh resolution*. Journal of the American Chemical Society 2006, 128, 2970-2976. PMC1544378

- Thomson Jodi M.; Prati Fabio; Bethel Christopher R.; Bonomo Robert A.\* *Use of novel boronic acid transition state inhibitors to probe substrate affinity in SHV-type extended-spectrum  $\beta$ -lactamases*. *Antimicrobial Agents and Chemotherapy* 2007, 51, 1577-1579. PMC1855462
- Morandi Stefania, Morandi Federica, Caselli Emilia, Shoichet Brian K., Prati Fabio\*. *Structure-based optimization of cephalotin analogue boronic acids as  $\beta$ -lactamase inhibitors*. *Bioorganic and Medicinal Chemistry*, 2008, 1195-1205. PMC2396669

The most potent beta-lactamases inhibitors displayed excellent *in vivo* activity in mice. Whereas cefotaxime alone failed to cure mice infected with highly resistant hospital-derived strain of *Escherichia coli*, they were cleared of infection when treated with cefotaxime:boronic acid combination. These molecules are not only inhibitor, but also molecular probes of the catalytic pocket; they are able to interact with the catalytic serine residue of the beta-lactamases acting as transition state analog. The complex boronic acid/beta-lactamase resembles the addition product of the nucleophilic substitution reaction occurring at the beta-lactam carbonyl. The X-ray structure of this complex allows for the comprehension of the role of each amino acid residue of the catalytic pocket along the reaction coordinate.

- Melissa Barnes, Magdalena Taracila, Joseph Rutter, Christopher Bethel, Ioannis Galdadas, Andrea Hujer, Emilia Caselli, Fabio Prati, John Dekker, Krisztina Papp-Wallace, Shozeb Haider, and Robert Bonomo. *Deciphering the evolution of cephalosporin resistance to ceftolozane-tazobactam in Pseudomonas aeruginosa*. *mBio* (Open Access) – Volume 9, Issue 6, 2018, Article number e02085-18. PMC6299481
- Alexandra Bouza; Hollister Swanson, Kali Smolen, Alison VanDine, Magdalena Taracila, Chiara Romagnoli, Emilia Caselli, Fabio Prati, Robert Bonomo, Rachel Powers, Bradley Wallar. *Structure-based analysis of boronic acids as inhibitors of Acinetobacter-derived cephalosporinase-7 (ADC-7), a unique class C  $\beta$ -lactamase*. *ACS – Infectious Diseases* – 2018, 325-336. PMC5981863
- Emilia Caselli, Chiara Romagnoli, Rachel Powers, Magdalena Taracila, Alexandra Bouza, Hollister Swanson, Kali Smolen, Francesco Fini, Bradley Wallar, Robert Bonomo, Fabio Prati. *Inhibition of Acinetobacter-Derived Cephalosporinase (ADC): Exploring the Carboxylate Recognition Site Using Novel  $\beta$ -Lactamase Inhibitors*. *ACS – Infectious Diseases* – 2018, 337-348. PMC5987196
- O. Eidam, C. Romagnoli, G. Dalmasso, S. Barelier, E. Caselli, R. Bonnet\*, B. K. Shoichet\* and F. Prati\* *Fragment-guided Design of Subnanomolar  $\beta$ -Lactamase Inhibitors Active in vivo*. *Proceedings of the National Academy of Sciences*, 17448-1753, 109 (43), 2012. PMC3491531

The synthetic challenges offered by the rational design of new boronic molecules fostered the development of new synthetic strategies, spanning from click chemistry (Copper-Catalyzed Azide-Alkyne Cycloaddition) to multicomponent reactions.

- Francesco Fini, Alessandro Zanni, Maria Luisa Introvigne, Mattia Stucchi, Emilia Caselli and Fabio Prati. *Straightforward synthesis of chiral non-racemic  $\alpha$ -boryl isocyanides*. *Organic and Biomolecular Chemistry* – 2021, 6687-669
- ML Introvigne, M Taracila, F Prati, E Caselli, RA Bonomo. *Alpha-triazolylboronic acids: a promising scaffold for effective inhibitors of KPCs*. *ChemMedChem*, 2020, 15(14), 1283-1288.
- E. Caselli, C. Romagnoli, R. Vahabi, M. Taracila, R.A. Bonomo, F. Prati. *Click Chemistry in Lead Optimization of Boronic Acids as  $\beta$ -Lactamases Inhibitors*. *J.Med.Chem* – 2015, 58(14), 5445-5458
- C. Romagnoli, E. Caselli and F. Prati. *Synthesis of 1,2,3-triazol-1-yl-methaneboronic acids via click chemistry: an easy access to a new potential scaffold in protease inhibition*. *EurJOC* 2015 – 1075-1083.
- Spaggiari Alberto; Vaccari Daniele; Davoli Paolo; Torre Giovanni; Prati Fabio. *A Mild Synthesis of Vinyl Halides and gem-Dihalides Using Triphenyl Phosphite-Halogen-Based Reagents*. *Journal of Organic Chemistry* 2007, 72, 2216-2219.

**Complete List of Published Work at:**

<http://personale.unimore.it/rubrica/pubblicazioni/fprati>

## Other

In September 2011 he founded TheraBor Pharmaceutical, an academic Spin Off company focused on the discovery of new therapeutic agents based on boronic acids.

## Bibliometric data.

*h*-index: 31 (Scopus, 27.04.2022)  
35 (Google Scholar, 27.04.2022)  
Citations: 2457 (Scopus, 27.04.2022)  
3142 (Google Scholar, 27.04.2022)

## Funded projects (last ten years)

Funding Institution: National Institute of Health (USA) Grant Number 2R01AI072219-11

Project title: Understanding  $\beta$ -Lactam Resistance in *Acinetobacter baumannii* – II°

Principal Investigator: Prof. Robert Bonomo, Case Western Reserve University, Cleveland (Ohio, USA)

Local coordinator: Prof. Prati Fabio

Amount assigned to UNIMORE US\$ 385.768

Funded period: September 2019 - August 2023

Funding Institution: National Institute of Health (USA) Grant Number 2R01AI063517-11A1

Project title: Challenges in beta-Lactamase Mediated Resistance

Principal Investigator: Prof. Robert Bonomo, Case Western Reserve University, Cleveland (Ohio, USA)

Local coordinator: Prof. Prati Fabio

Amount assigned to UNIMORE: US\$ 391.023

Funded period: January 2019 - December 2023

Funding Institution: National Institute of Health (USA), Grant Number: 2R01AI072219-06A1

Project title: Understanding  $\beta$ -Lactam Resistance in *Acinetobacter baumannii*

Principal Investigator: Prof. Robert Bonomo, Case Western Reserve University, Cleveland (Ohio, USA)

Local coordinator: Prof. Prati Fabio

Amount assigned to UNIMORE: US\$ 226.045

Funded period: Jun 2014 - Mar 2019

Funding institution: Harrington Discovery Institute (Cleveland, OH, USA)

Project title: Development of Novel Agents to Treat Emerging Infectious Diseases Threats

Principal Investigator: Prof. Robert Bonomo, Case Western Reserve University, Cleveland (Ohio, USA)

Local coordinator: Prof. Prati Fabio

Amount assigned to UNIMORE: US\$ 100.000

Funded period: Jan 2015 – Dec 2016

Funding institution: National Institute of Health (USA), 1R15AI094489-01

Funding Institution: National Institute of Health (USA), 2 R01 AI063517-06A1

Project title: Challenges in beta-Lactamase Mediated Resistance

Principal Investigator: Prof. Robert Bonomo, Case Western Reserve University, Cleveland (Ohio, USA)

Local coordinator: Prof. Prati Fabio

Amount assigned to UNIMORE: US\$ 200.000

Funded period: Jun 2010-May 2015

Funding institution: National Institute of Health (USA), GM63815

Research title: Structure, Function and Inhibition of beta-Lactamases III

Principal Investigator: Prof. B. Shoichet, University of California San Francisco

Local coordinator: Prof. Prati Fabio

Amount assigned to UNIMORE: US\$ 184.000

Funded period: Apr 2010-Mar 2014

Modena, April 27, 2022