

Refaat B. Hamed, DPhil (Oxon)

Department of Pharmacognosy,
Faculty of Pharmacy, Assiut University,
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Education

University of Oxford, Department of Chemistry

DPhil (Organic Chemistry)

Supervisors: Prof. Christopher J. Schofield, Prof. Timothy D. W. Claridge

Thesis Title: “*Biocatalytic and Mechanistic Studies on Carbapenem Biosynthesis Enzymes*”.

08-2006 to
04-2010

Assiut University (Egypt), Faculty of Pharmacy

Master of Science (Natural Products Chemistry)

Supervisors: Prof. A. M. El-Moghazy, Prof. S. M. El-Sayyad, Prof. M. S. Kamel

Thesis Title: “*Pharmacognostical study of Podranea ricasoliana (Tanfani) Sprague Family Bignoniaceae cultivated in Egypt*”.

04-2001 to
03-2004

Bachelor of Science with highest honors in Pharmaceutical Sciences.

09-1995 to
06-1999

University of Illinois at Urbana–Champaign

Department of Chemical & Biomolecular Engineering

Senior Postdoctoral Research Fellow

I used biocatalysis, biosynthesis, protein engineering, and metabolic engineering for synthesis of high value chemicals. Particularly, I targeted redesign of P450 proteins to catalyze new chemical transformations involving carbene, nitrene and oxene transfer.

06-2013 to
04-2014

University of Oxford, Department of Chemistry

Postdoctoral Research Fellow

I carried out biosynthetic, mechanistic, structural, protein engineering and biocatalytic studies on a variety of enzymes, including some involved in β -lactam antibiotics Biosynthesis. I developed bioanalytical approaches (mainly NMR and MS-based) for (real-time) monitoring of enzymatic and non-enzymatic reactions.

03-2010 to
06-2013

Assiut University (Egypt), Faculty of Pharmacy

Department of Natural Products Chemistry (Pharmacognosy)

Assistant Professor of Natural Products Chemistry

AI am currently involved in research and teaching focusing on biotechnological approaches of production of natural products (e.g. tissue culture, microbial biotransformation and molecular biopharming).

06-2011
Current position

Assistant Lecturer (on leave between 08/2006 to 05/2011)

04-2004 to

Demonstrator of Natural Products Chemistry

05-2011

I conducted research and undergraduate teaching that focused on isolation, structural elucidation, and biological evaluation of natural products.

12-1999 to
04-2004

Employment

H-Index = 12, Total Number of Citations = 371 (Since 2008)

Reviews

1. **Hamed, R. B.**,* Gomez-Castellanos, J. R., Henry, L., Ducho, C., McDonough, M. A., and Schofield, C. J.* (2013) The enzymes of β -lactam biosynthesis, *Nat. Prod. Rep.* 30, 21-107.

- This is the first comprehensive review covering the enzymology of the β -lactam biosynthesis.
- It has been featured on the cover of *Nat. Prod. Rep.* (Issue 1, 2013).

2. **Hamed, R. B.**, Batchelar, E. T., Clifton, I. J., and Schofield, C. J. (2008) Mechanisms and structures of crotonase superfamily enzymes – How nature controls enolate and oxyanion reactivity, *Cell. Mol. Life Sci.* 65, 2507-2527.

- This review, covering crotonase catalysis, has been cited >50 times in the past four years.

3. **Hamed, R. B.**,* Henry, L., Gomez-Castellanos, J. R., Asghar, A., Brem, J., Claridge, T. D. W., and Schofield, C. J.* (2013) Stereoselective preparation of lipidated carboxymethyl-proline and pipercolic acid derivatives via coupling of engineered crotonases with alkylmalonyl-CoA synthetases, *Org. Biomol. Chem.* 11, 8191-8196.

4. Mantri, M., Webby, C. J., Loik, N. D., **Hamed, R. B.**, Nielsen, M. L., McDonough, M. A., McCullagh, J. S. O., Bottger, A., Schofield, C. J., and Wolf, A. (2012) Self-hydroxylation of the splicing factor lysyl hydroxylase, JMJD6, *MedChemComm* 3, 80-85.

5. **Hamed, R. B.**, Henry, L., Gomez-Castellanos, J. R., Mecinović, J., Ducho, C., Sorensen, J. L., Claridge, T. D. W., and Schofield, C. J. (2012) Crotonase Catalysis Enables Flexible Production of Functionalized Prolines and Carbapenams, *J. Am. Chem. Soc.* 134, 471-479.

- This is the first paper to demonstrate the amenability of carbapenem biosynthesis pathways to engineering for the production of new carbapenams. The paper was described by reviewers as the first true advance in the field over the past three decades.
- The work demonstrates the power of protein engineering to enable stereoselective formation of a multiplicity of functionalized *N*-heterocycles, including ones with “quaternary” carbons.

6. Ge, W., Wolf, A., Feng, T., Ho, C.-h., Sekirnik, R., Zayer, A., Granatino, N., Cockman, M. E., Loenarz, C., Loik, N. D., Hardy, A. P., Claridge, T. D. W., **Hamed, R. B.**, Chowdhury, R., Gong, i., Robinson, C. V., Trudgian, D. C., Jiang, M., Mackeen, M. M., McCullagh, J. S., Gordiyenko, Y., Thalhammer, A., Yamamoto, A., Yang, M., Liu-Yi, P., Zhang, Z., Schmidt-Zachmann, M., Kessler, B. M., Ratcliffe, P. J., Preston, G. M., Coleman, M. L., and Schofield, C. J. (2012) Oxygenase Catalysed Ribosome Hydroxylation Occurs in Prokaryotes and Humans, *Nat. Chem. Biol.* 8, 960-962.

7. Yang, M., Chowdhury, R., Ge, W., **Hamed, R. B.**, McDonough, M. A., Claridge, T. D. W., Kessler, B. M., Cockman, M. E., Ratcliffe, P. J., and Schofield, C. J. (2011) Factor-inhibiting hypoxia-inducible factor (FIH) catalyses the post-translational hydroxylation of histidiny residues within ankyrin repeat domains, *FEBS J.* 278, 1086-1097.

8. Rotili, D., Altun, M., **Hamed, R. B.**, Loenarz, C., Thalhammer, A., Hopkinson, R. J., Tian, Y.-M., Ratcliffe, P. J., Mai, A., Kessler, B. M., and Schofield, C. J. (2011) Photoactivable peptides for identifying enzyme-substrate and protein-protein interactions, *Chem. Commun.* 47, 1488-1490.

9. Mantri, M., Loik, N. D., **Hamed, R. B.**, Claridge, T. D. W., McCullagh, J. S. O., and Schofield, C. J. (2011) The 2-Oxoglutarate-Dependent Oxygenase JMJD6 Catalyses Oxidation of Lysine Residues to give 5S-Hydroxylysine Residues, *ChemBioChem* 12, 531-534.

10. **Hamed, R. B.**, Gomez-Castellanos, J. R., Thalhammer, A., Harding, D., Ducho, C., Claridge, T. D. W., and Schofield, C. J. (2011) Stereoselective C–C bond formation catalysed by engineered carboxymethylproline synthases, *Nat. Chem.* 3, 365-371.

- This paper, together with no. 3, represents the first demonstration of near complete control of “Enolate” formation and/or reactivity employing (engineered) biocatalysts.

11. Hopkinson,[†] R. J., **Hamed, R. B.**,[†] Rose, N. R.,[†] Claridge, T. D. W., and Schofield, C. J. (2010) Monitoring the Activity of 2-Oxoglutarate Dependent Histone Demethylases by NMR Spectroscopy: Direct Observation of Formaldehyde, *ChemBioChem* 11, 506-510.

- This paper is one of a series (see also no. 4, 6, 7, 9, 13, and 14) where I developed (real-time) NMR methods to monitor enzymatic and non-enzymatic reactions. Many of the substrates/products of the monitored reactions (e.g. formaldehyde) are difficult to detect otherwise.

Publications

Research Articles

[†]Joint first author, *Corresponding author

12. Hamed, R. B., Mecinovic, J., Ducho, C., Claridge, T. D. W., and Schofield, C. J. (2010) Carboxymethylproline synthase catalysed syntheses of functionalised *N*-heterocycles, *Chem. Commun.* 46, 1413-1415.

- This paper was highlighted in “Hot off the Press” in *Nat. Prod. Rep.*, 2010, 27, 805-808.

13. Flashman, E., Hoffart, L. M., Hamed, R. B., Bollinger Jr, J. M., Krebs, C., and Schofield, C. J. (2010) Evidence for the slow reaction of hypoxia-inducible factor prolyl hydroxylase 2 with oxygen, *FEBS J.* 277, 4089-4099.

14. Mecinović, J., Hamed, R. B., and Schofield, C. J. (2009) Iron-mediated cleavage of C-C bonds in vicinal tricarbonyl compounds in water, *Angew. Chem. Int. Ed.* 48, 2796-2800.

15. Hamed, R. B., Batchelar, E. T., Mecinovic, J., Claridge, T. D. W., and Schofield, C. J. (2009) Evidence that Thienamycin Biosynthesis Proceeds via C-5 Epimerization: ThnE Catalyzes the Formation of (2*S*,5*S*)-*trans*-Carboxymethylproline, *ChemBioChem* 10, 246-250.

- This paper was featured on the cover of *ChemBiochem* Volume 10, Issue 2.

16. Ducho, C., Hamed, R. B., Batchelar, E. T., Sorensen, J. L., Odell, B., and Schofield, C. J. (2009) Synthesis of regio- and stereoselectively deuterium-labelled derivatives of L-glutamate semialdehyde for studies on carbapenem biosynthesis, *Org. Biomol. Chem.* 7, 2770-2779.

17. Batchelar, E. T.,[†] Hamed, R. B.,[†] Ducho, C., Claridge, T. D. W., Edelmann, M. J., Kessler, B., and Schofield, C. J. (2008) Thioester hydrolysis and C-C bond formation by carboxymethylproline synthase from the crotonase superfamily, *Angew. Chem. Int. Ed.* 47, 9322-9325.

18. El-Moghazy, A. M., El-Sayyad, S. M., Kamel, M. S., and Hamed, R. B. (2003) Chemical study of *Podranea ricasoliana* cultivated in Egypt, In 44th Annual Meeting of American Society of Pharmacognosy, *American Society of Pharmacognosy*, Chapel Hill, North Carolina, USA.

Schofield, C. J., Hamed, R. B., Batchelar, E. T., and Ducho, C. (2010) Methods for preparing heterocyclic rings, (Organization, W. I. P., Ed.), *WO Patent* WO/2010/046,713.

Hamed, R. B., Gomez-Castellanos, J. R., Henry, L., Claridge, T. D. W., and Schofield, C. J. Crotonase-catalysed Mutual Dynamic Kinetic Asymmetric C-C Bond Formation: Enzymic Control of Three Contiguous Stereocentres.

Hamed, R. B., Henry, L., Gomez-Castellanos, J. R., Claridge, T. D. W., and Schofield, C. J. New carbapenams by (engineered) carbapenem biosynthesis pathway enzymes.

- DPhil scholarship from the Egyptian Ministry of Higher Education 2006
- T3A Pharma Award for Top Ten Graduate Students (Egypt) 2000
- EIPICO Award for Distinguished Graduate Students (Egypt) 2000
- CID Pharmaceuticals Award for Distinguished Graduate Students (Egypt) 1999
- SEDICO Pharmaceutical CO. Award (Egypt) 1999

- From Protein Posttranslational Modification and Engineering to Antibiotic Biosynthesis
The School of Biological and Chemical Sciences, Queen Mary University of London 2013
- The Biocatalytic Versatility of Wildtype and Engineered Carboxymethylproline Synthases
Assiut University 8th International Pharmaceutical Sciences Conference 2012
- (Stereoselective) Biocatalytic Production of Natural and Unnatural Products
Chemistry Department, University of Southampton 2011
- Monitoring the activities of the crotonase superfamily enzymes by ¹H-NMR in real time
RSC NMR Discussion Group “Postgraduate Meeting” 2009

- University of Oxford, Department of Chemistry 2006-2010
Organic Chemistry Laboratory Demonstrator
- University of Oxford, St Edmund Hall 2009-2010
Chemical Biology Tutor
- Assiut University, Faculty of Pharmacy 1999-2006
Natural Products Chemistry Tutor and Laboratory Demonstrator