



Peptides 2008

*Chemistry of Peptides in Life Science,
Technology and Medicine*

*Proceedings of
The Thirtieth European Peptide Symposium*

*Edited by
Hilkka Lankinen*

FIPS 
Finnish Peptide Society
Societas Biochemica, Biophysica et Microbiologica Fenniae



ISBN 978-952-92-5198-8

Copyright © 2008 The Finnish Peptide Society and The European Peptide Society

Published by The Finnish Peptide Society

Layout and Cover design by Timo Päivärinta, PSWFolders Ltd

Manuscripts collected by CONGREX / Blue & White Conferences Oy using Abstractlogic®

All rights reserved. No part of this book may be reproduced or transmitted in any form by any means, mechanical, electronic, photocopying, recording or otherwise without the written permission of the copyright holder.

Produced in Finland

1-01-111

Photoinduced macrocyclizations on helical Bpa/Met oligopeptides

Moretto, Alessandro¹; Crisma, Marco¹; Formaggio, Fernando¹; Huck, Lawrence A.²; Mangion, Dino²; Leigh, William J.²; Toniolo, Claudio¹

¹University of Padova, 35131 Padova, ICB-CNR, Padova Unit, Department of Chemistry, ITALY; ²McMaster University, Hamilton, ON, L8S 4M1, Department of Chemistry, CANADA

¹E-mail: alessandro.moretto.1@unipd.it

The [3-(4-benzoylphenyl)alanine] (Bpa) residue is widely used as a photoaffinity label for the study of *intermolecular* (peptide) ligand-protein (receptor) interactions, where it is thought to primarily function by hydrogen-abstraction from Met residues followed by covalent C-C bond formation of the resulting radical pair.^{1,2}

We are carrying out detailed studies of this reaction in a series of five, structurally rigid, 3_{10} -helical hexapeptides of general sequences Boc-U_xBU_yMU_z-OMe and Boc-U_xMU_yBMU_z-OMe, where B = L-Bpa, U = Aib, M = L-Met, and U_x+U_y+U_z = 4. We aim at determining the effects of spacer length (U_y = 1-3) on the rate of the intramolecular excited state reaction (Yang photocyclization) and the chemical and 3D-structures of the resulting products. The triplet state lifetimes of the Bpa residues in the compounds, determined in a deoxygenated, dilute, CH₃CN solution by laser flash photolysis, vary in the following order: UBU₂MU, τ = 60 ns; UMU₂BU, τ = 190 ns; UBUMU₂, τ = 350 ns; UBMU₃, τ = 430 ns; and UBU₃M, τ = 920 ns.

In addition to the information these data provide on the structural requirements for intramolecular excited state quenching in the molecules, they also serve to define the conditions necessary for optimal intramolecular reaction in preparative photolysis experiments. Accordingly, the products resulting from UBU₂MU have been prepared in high yields, isolated, and structurally characterized by HPLC, mass spectrometry, FT-IR absorption, NMR, and CD techniques, and for one of them by X-ray diffraction as well (Fig. 1).

Two 3_{10} -helical diastereomers, arising exclusively from the Bpa diradical regioselective attack on the Met S-methyl group (Fig. 2), were found.

References

1. Kauer J.C., Erickson-Viitanen S., Wolfe H. R. Jr., DeGrado W.F., J. Biol. Chem. **261**: 10695-10700, 1986.
2. Pérodin J., Deraët M., Auger-Messier M., Boucard A.A., Rihakova L., Beaulieu M.-E., Lavigne P., Parent J.-L., Guillemette G., Leduc R., Escher E., Biochemistry **41**: 14348-14356, 2002.

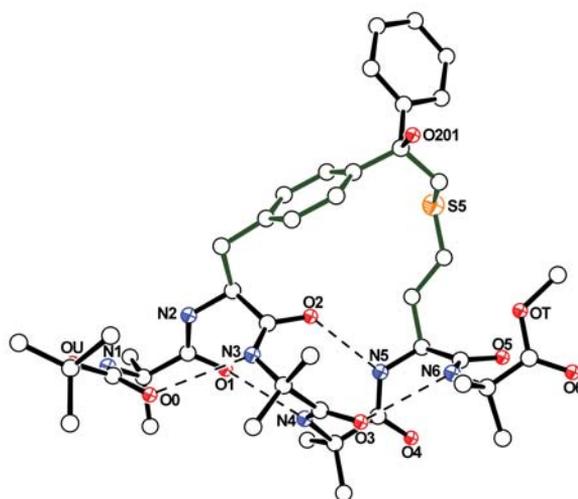


Figure 1. X-Ray diffraction structure of the major side-chain conformer of the macrocyclized hexapeptide diastereomer (product **B**) arising from the Yang photocyclization of Boc-Aib-L-Bpa-(Aib)₂-L-Met-Aib-OMe. The configuration of the novel side-chain chiral center is R. H-atoms have been omitted. Only the N, O, and S atoms are numbered. The three C=O...H-N intramolecular H-bonds of the 3_{10} -helical structure are represented by dashed lines.

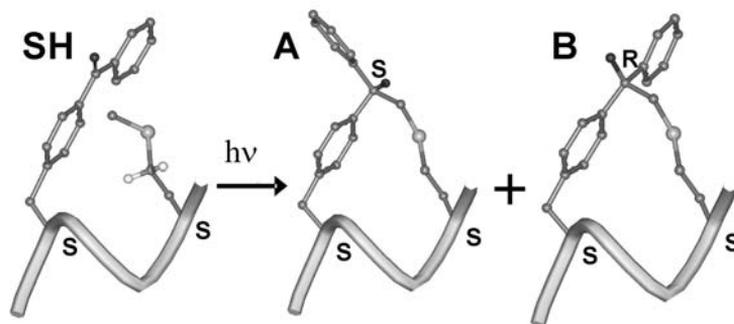


Figure 2. Cartoon showing the two diastereomeric products (A and B) afforded by the Yang photocyclization reaction on the terminally-protected hexapeptide Boc-Aib-L-Bpa-(Aib)₂-L-Met-Aib-OMe (SH). H-abstraction took place only from the Met ϵ -CH₃ group.