

Supporting Information

**A Rapid and Clean Synthetic Approach for Cyclic Peptides via
Micro-flow Peptide Chain Elongation and Photochemical Cyclization:
Synthesis of Cyclic RGD Peptide**

Yuto Mifune, Hiroyuki Nakamura and Shinichiro Fuse*

*Laboratory for Chemistry and Life Science, Institute of Innovative Research, Tokyo Institute of Technology,
4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8503, Japan. E-mail: sfuse@res.titech.ac.jp*

Table of Contents

1. Micro-flow reactor setup	S-2
2. NMR spectra	S-4

1. Micro-flow reactor setup

The employed micro-flow system for amide bond formation is shown in Figure S-1. Stainless steel T-shape mixers were purchased from Sanko Seiki Co. Ltd. (inner diameter: 0.25 mm). Teflon[®] tube with inner diameter 0.8 mm was purchased from Senshu Scientific Co. Ltd. The T-shape mixers and Teflon[®] tube were connected with PEEK fittings purchased from GL Science Co. Ltd. Solutions were introduced to micro-flow system with the syringe pumps (Harvard Pump 11 and Harvard PHD ULTRA) equipped gastight syringes (SGE). The gastight syringes and Teflon[®] tube were connected with joints purchased from Techno Applications Co. Ltd. The gastight syringes and T-shape mixers 1 and 2 were connected with Teflon[®] tube (inner diameter: 0.8 mm, length: 800 mm, volume 402 μ L). T-shape mixers 1 and 2 were connected with reaction tube 1 (Teflon[®] tube). T-shape mixer 2 was connected with reaction tube 2 (Teflon[®] tube). The reaction tube 2 and Teflon[®] tube (inner diameter: 0.25 mm, length 100 mm, volume 5 μ L) were connected to generate back pressure. T-shape mixers and reaction tube were immersed in water bath.

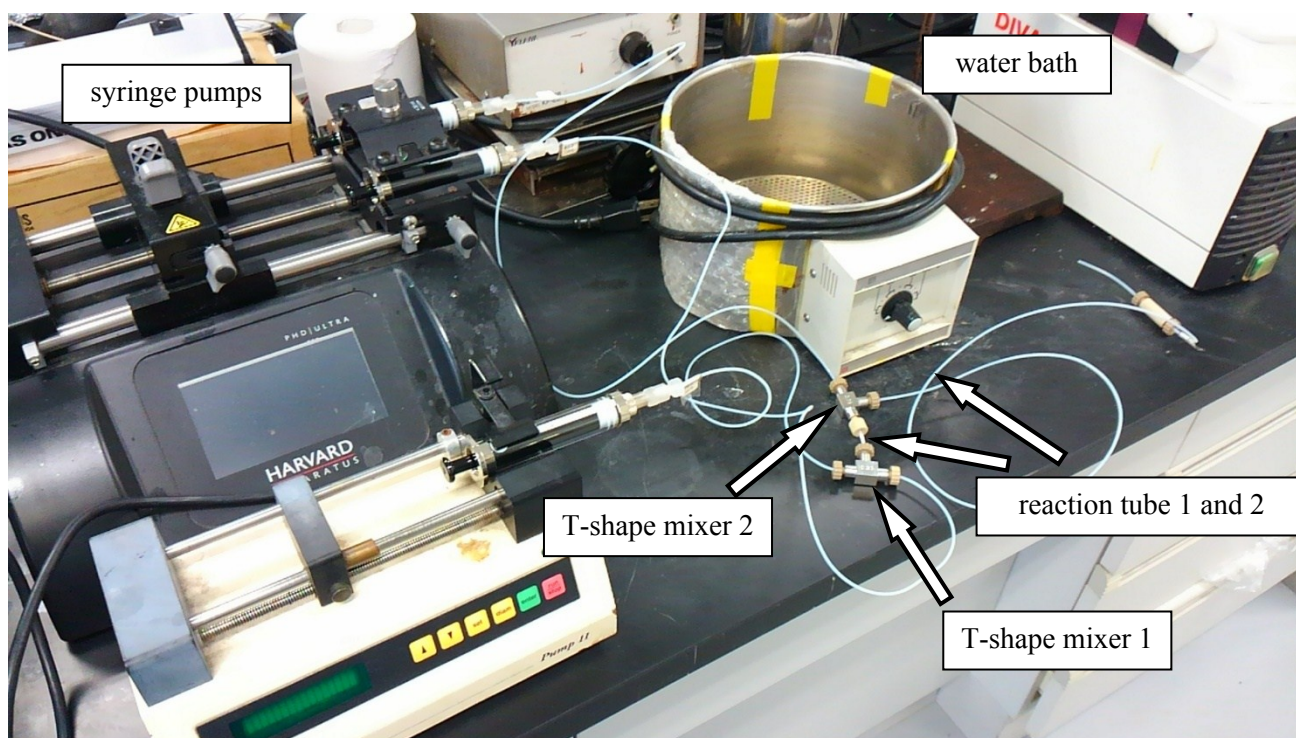


Figure S-1

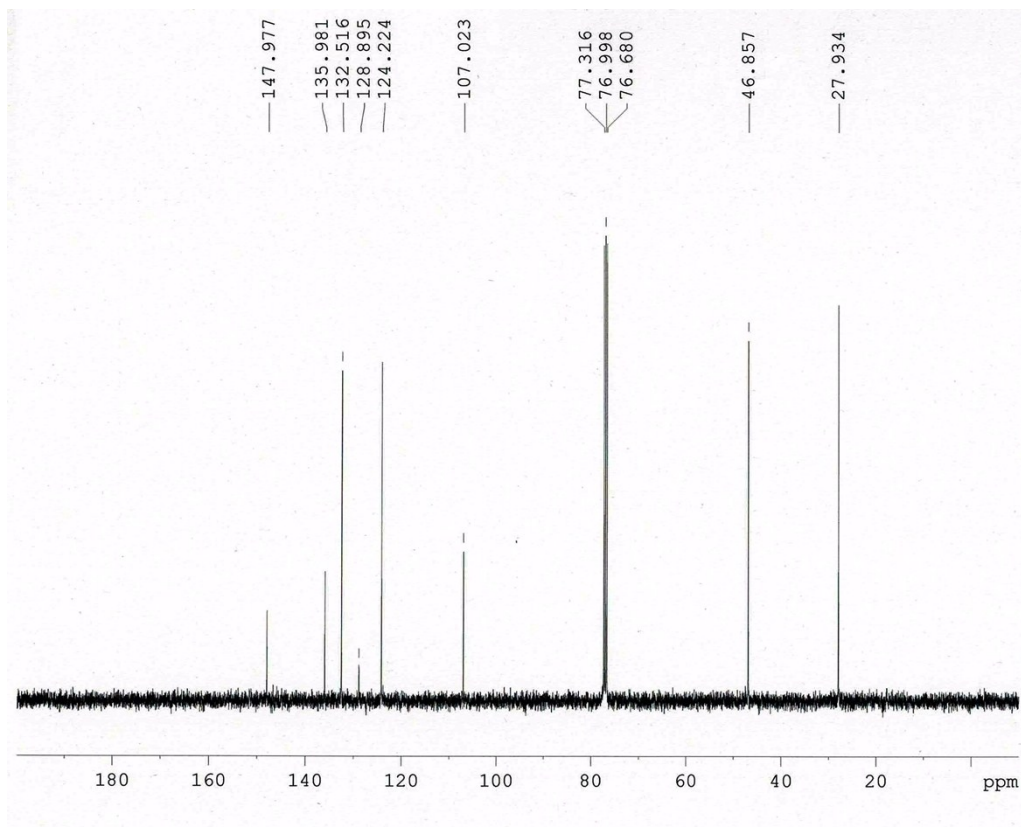
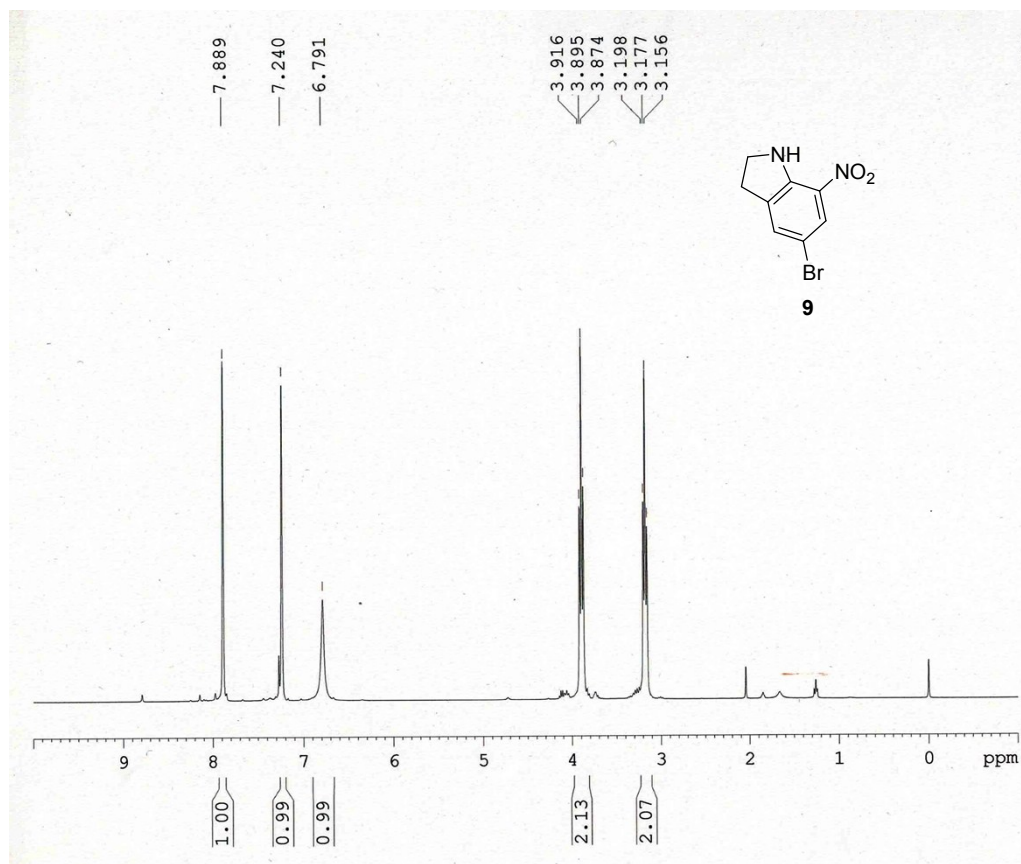
The employed micro-flow system for photochemical cyclization is shown in Figure S-2. 9 W UV lamp (wavelength: 365 nm) were purchased from AS ONE Co., Ltd. A fluorinated ethylene propylene copolymer (FEP) tube (Flon Industry Co., Ltd., inner diameter: 1.0 mm) was used as the tube reactor. The tube reactor was tightly wrapped around the lamp. Solution was introduced to the micro-flow system via syringe pump (Harvard PHD ULTRA) equipped with gastight syringe (SGE). The reactor and gastight syringe were connected by PEEK tubing (inner diameter: 0.5 mm). The tube reactor and lamp were wrapped in aluminum foil (not shown in figure).



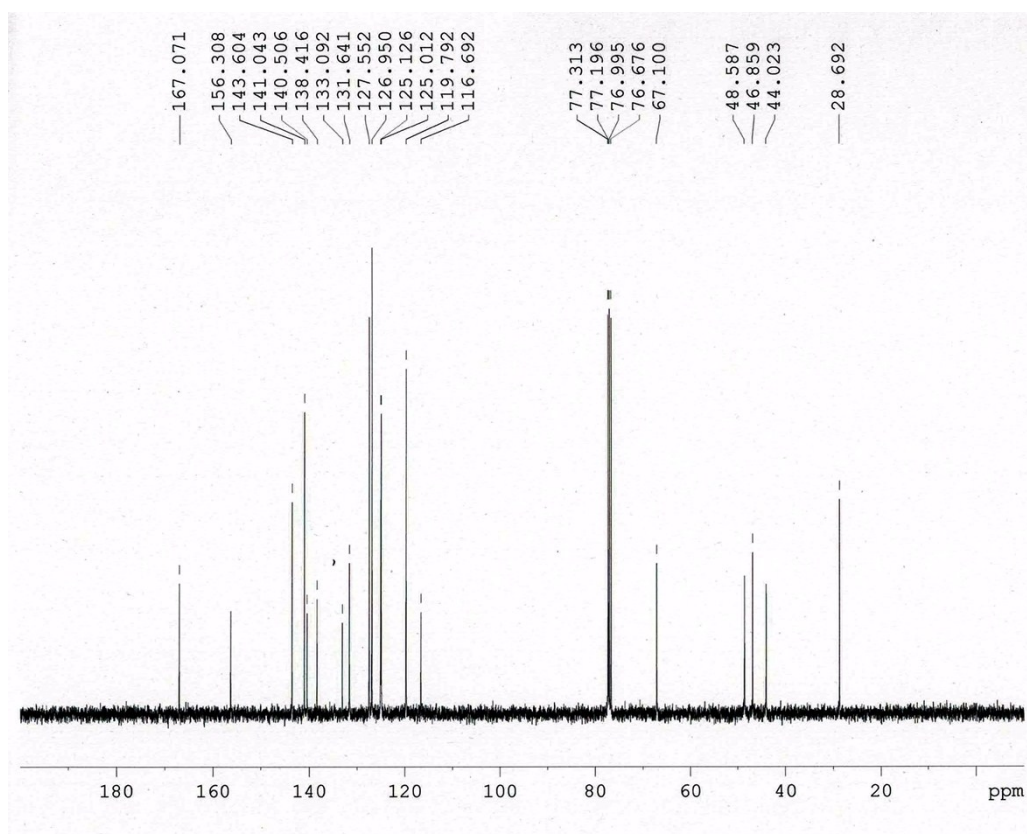
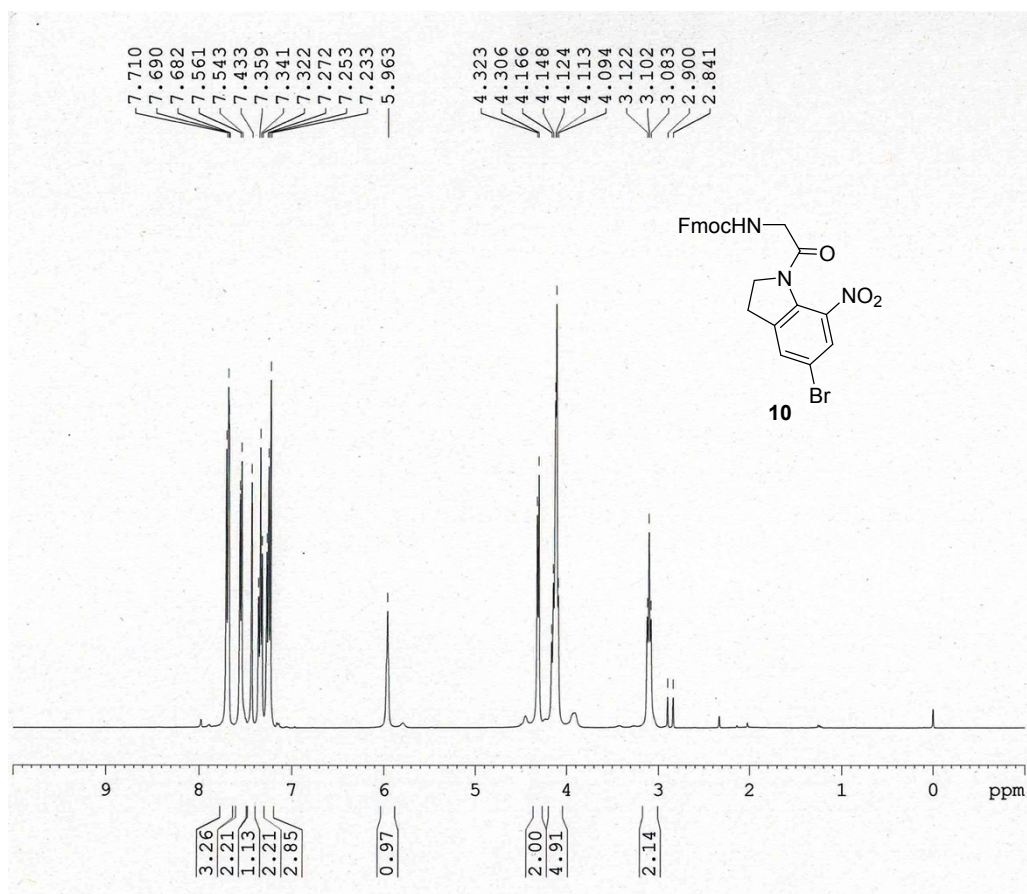
Figure S-2

2. NMR spectra

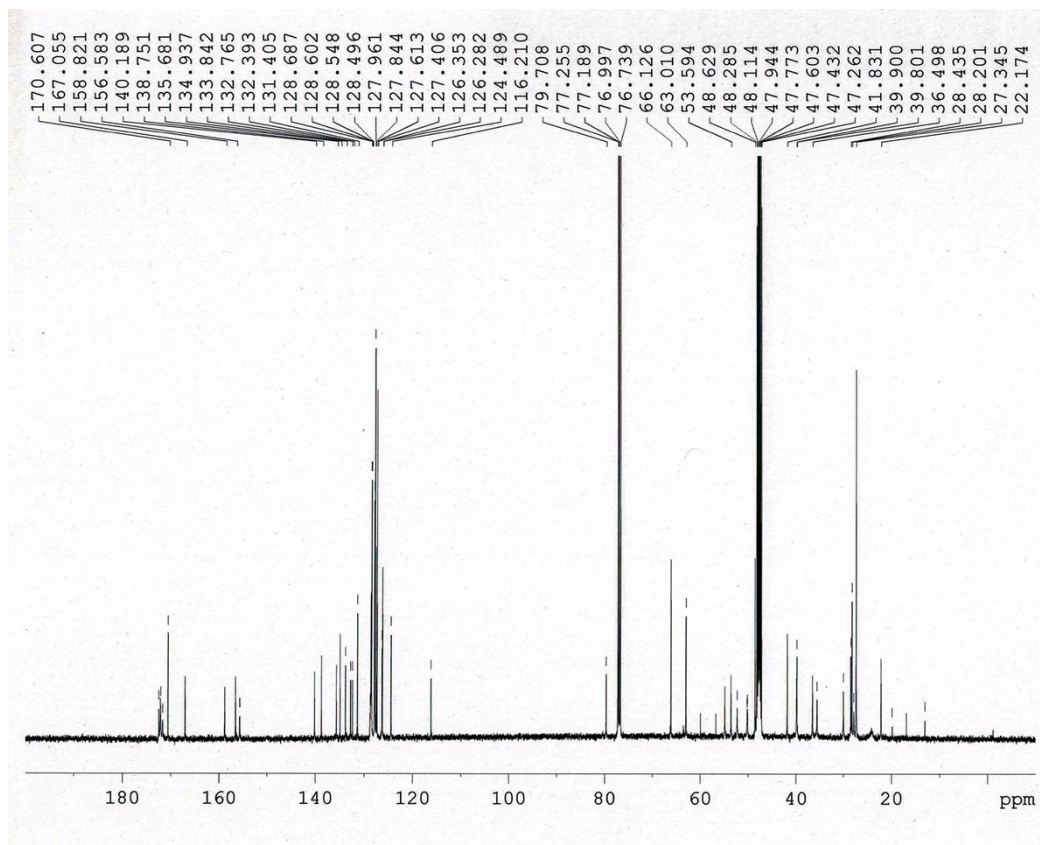
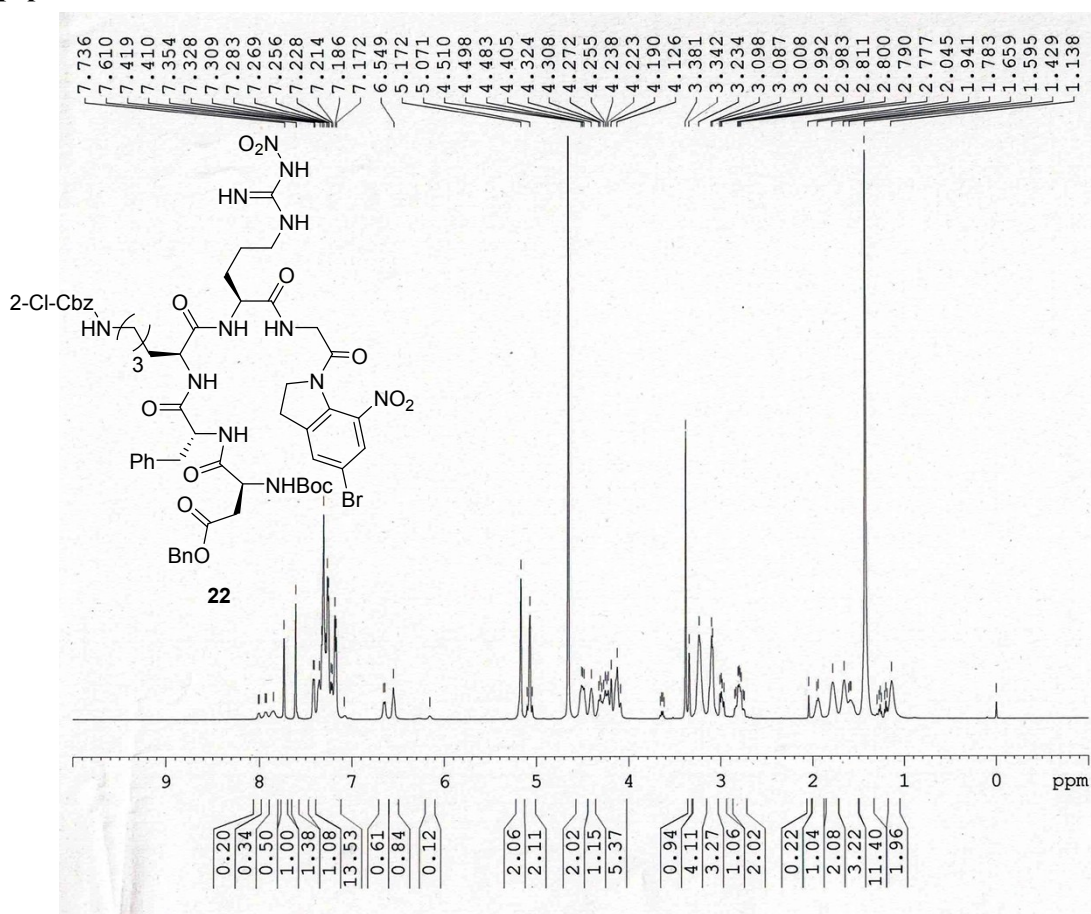
5-bromo-7-nitroindoline (Bni) (9)



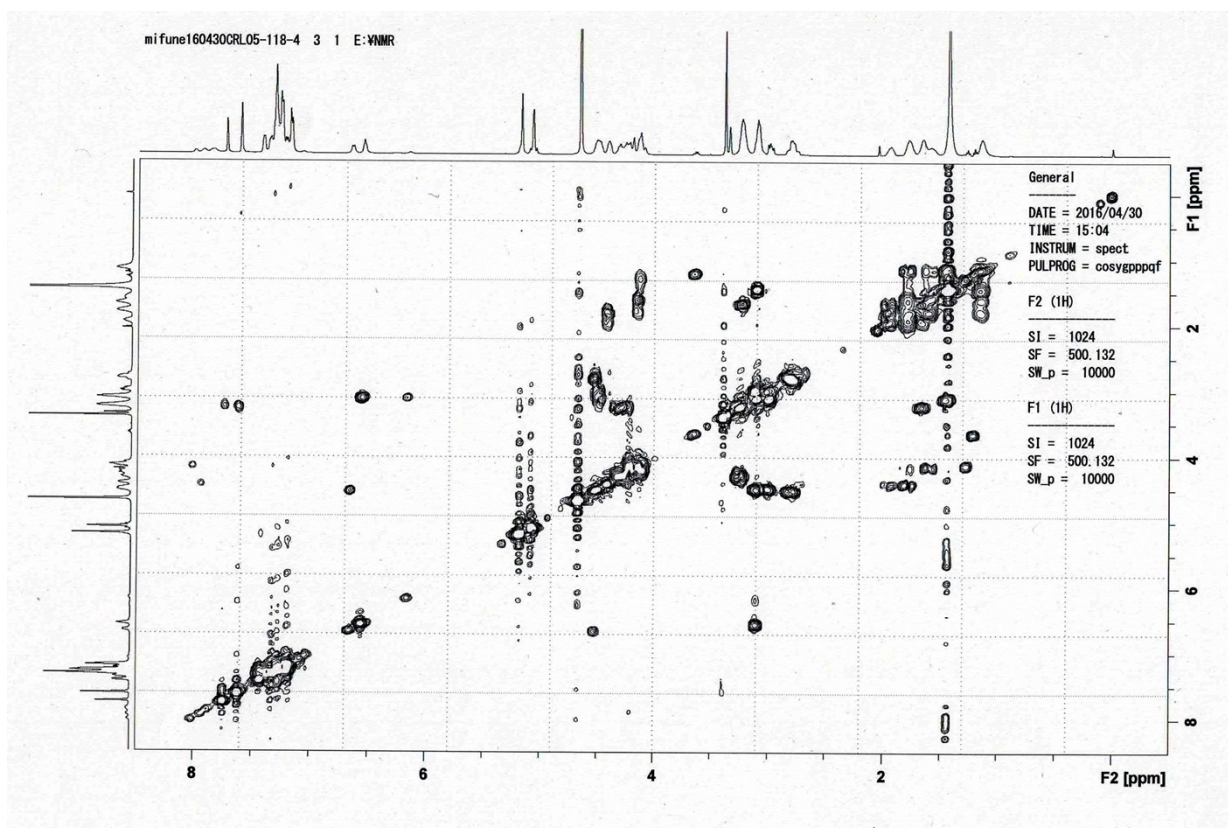
Bni-protected *N*-Fmoc-glycine 10



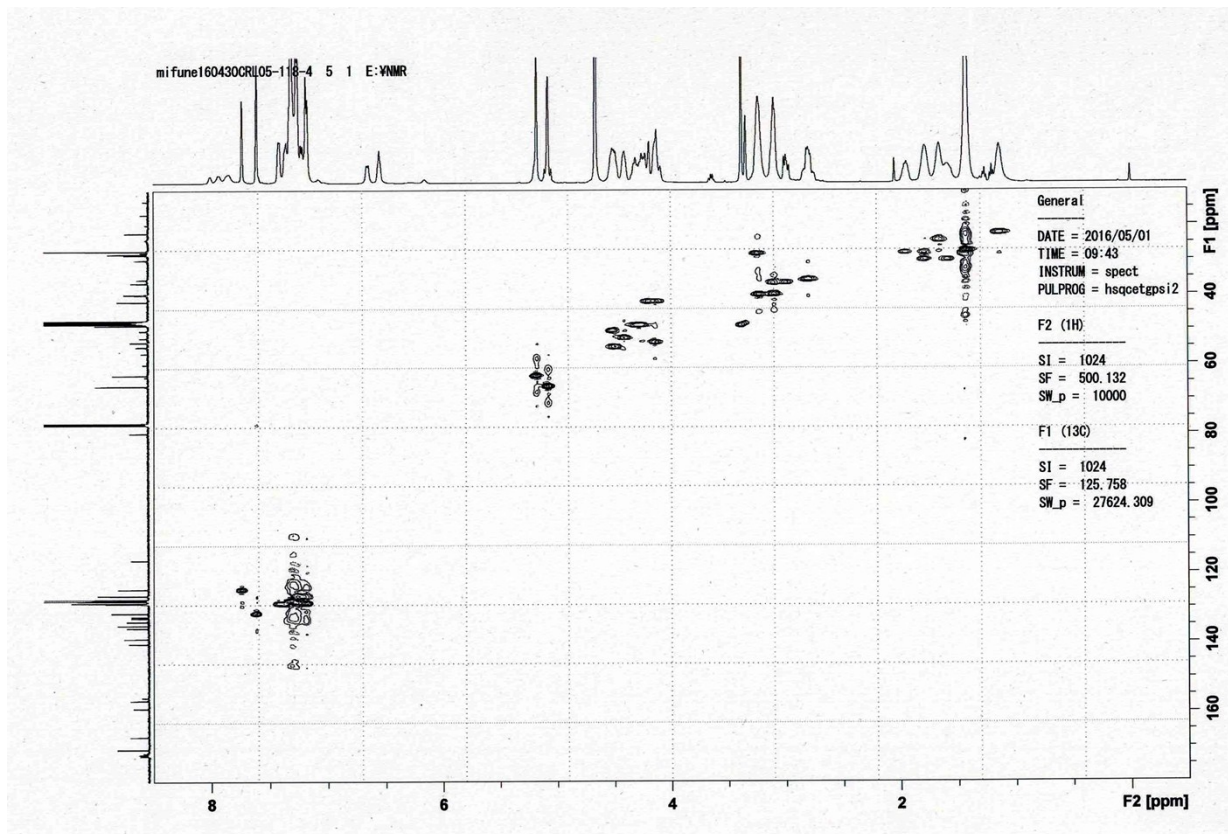
Pentapeptide 22



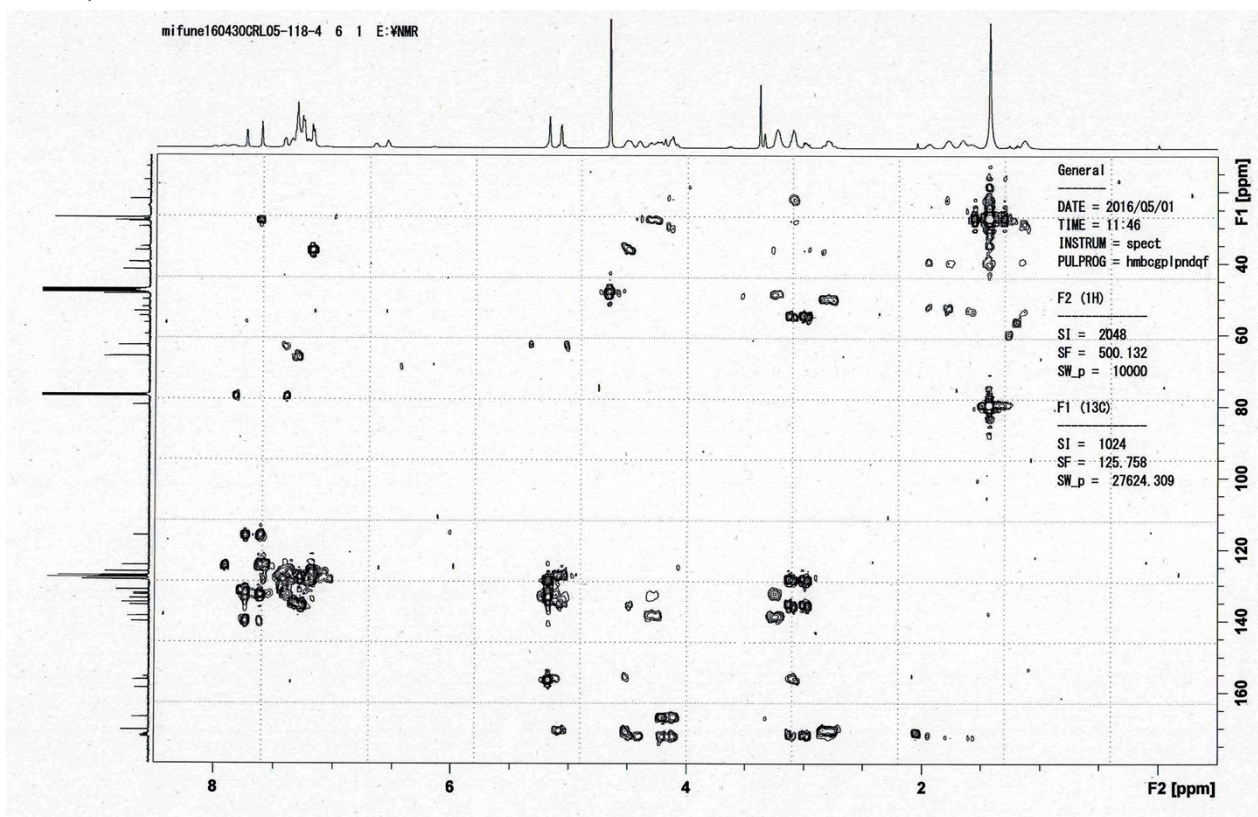
(¹H-¹H COSY)



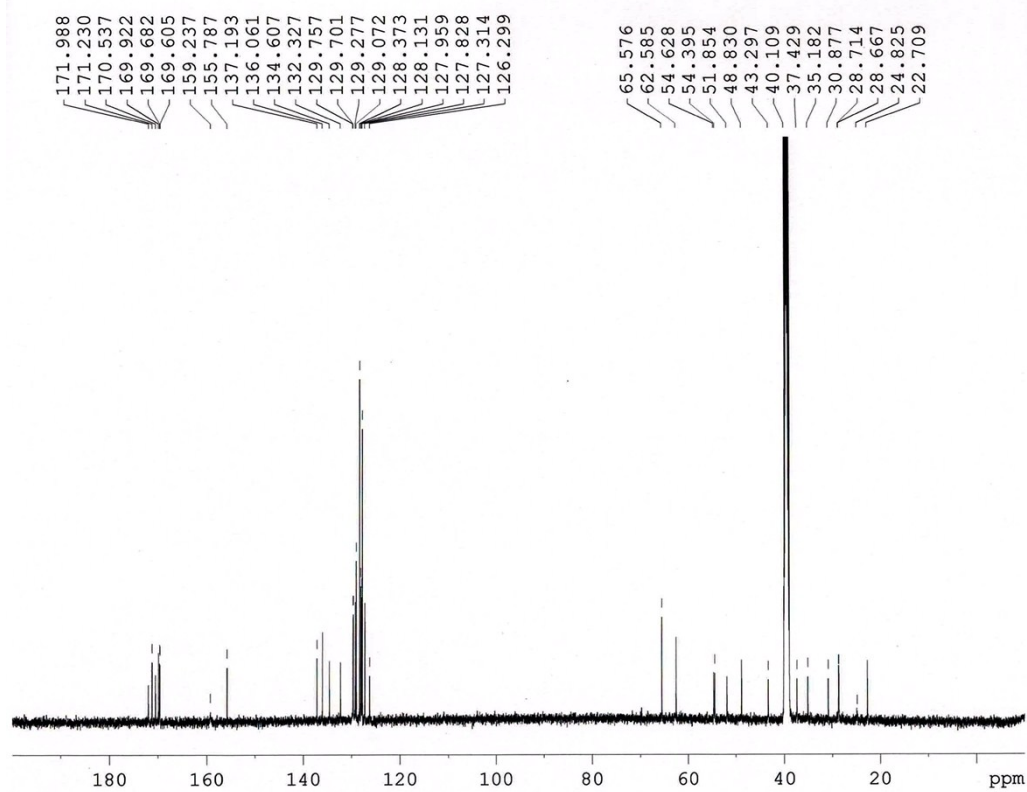
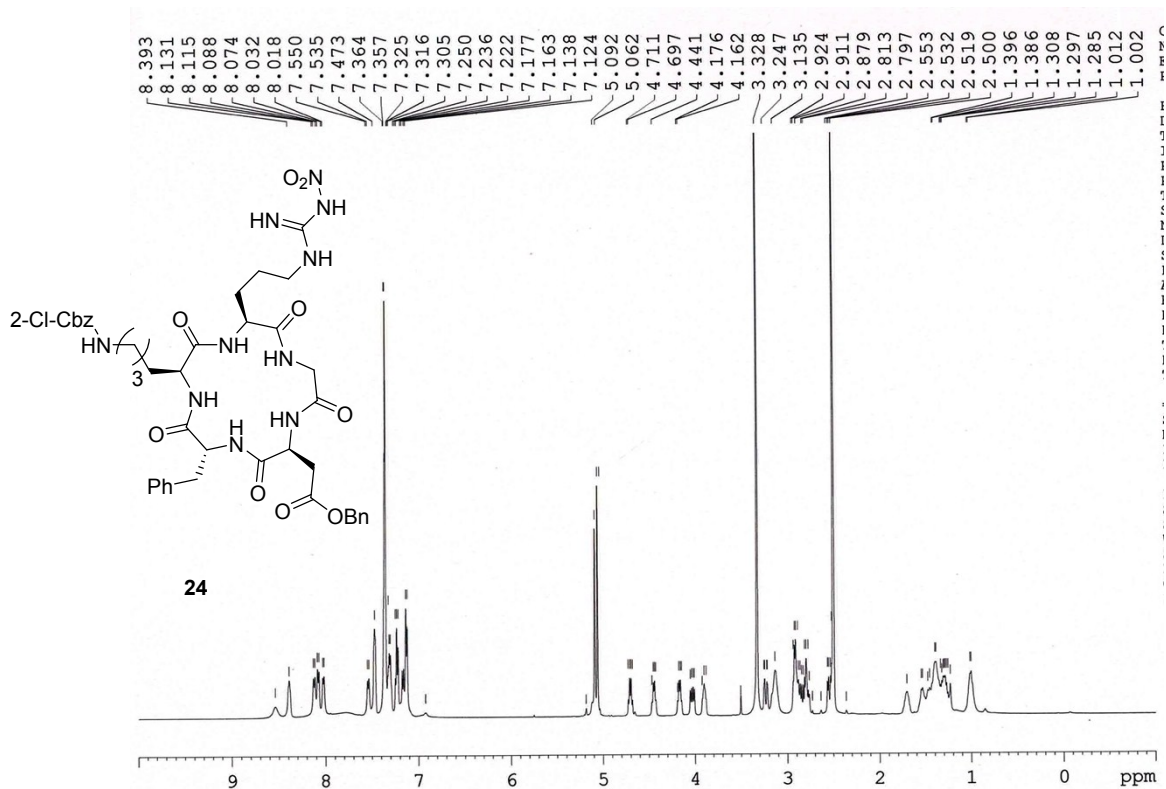
(HSQC)



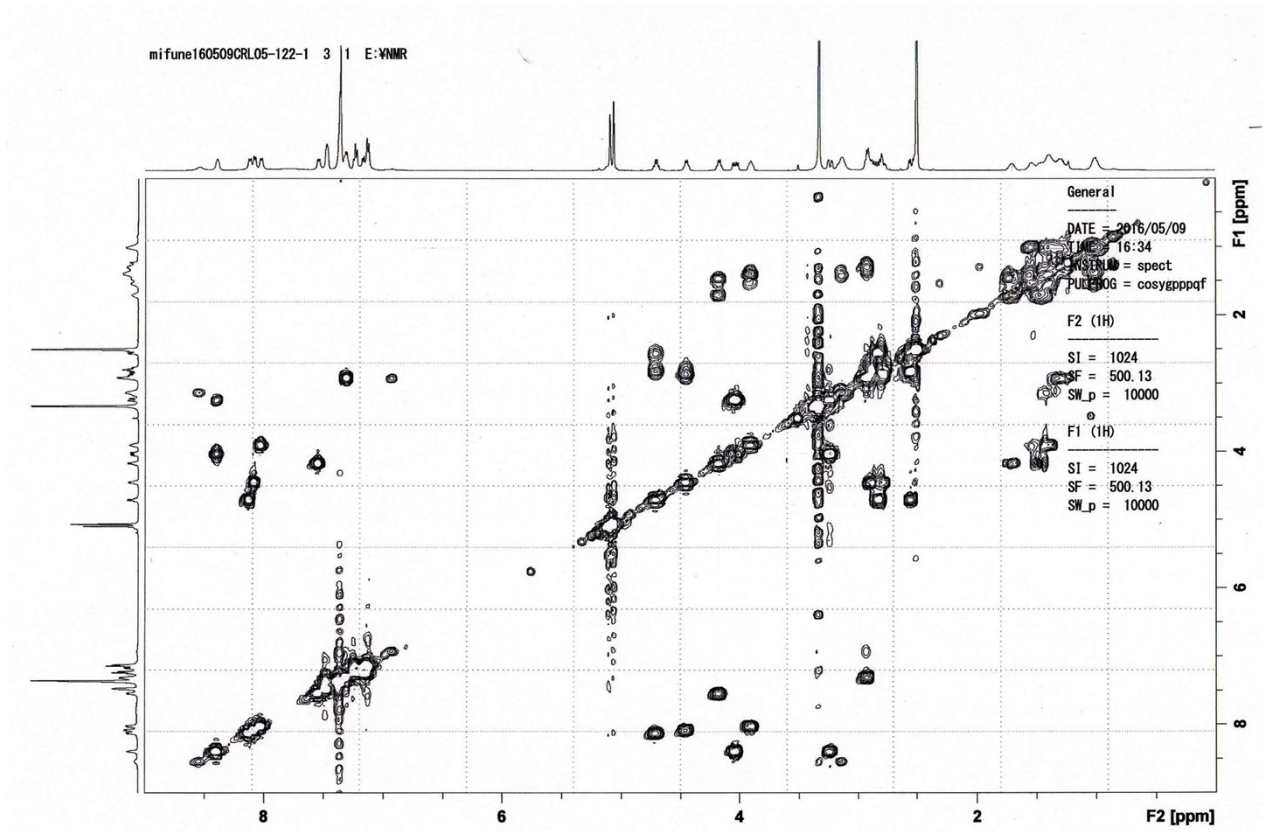
(HMBC)



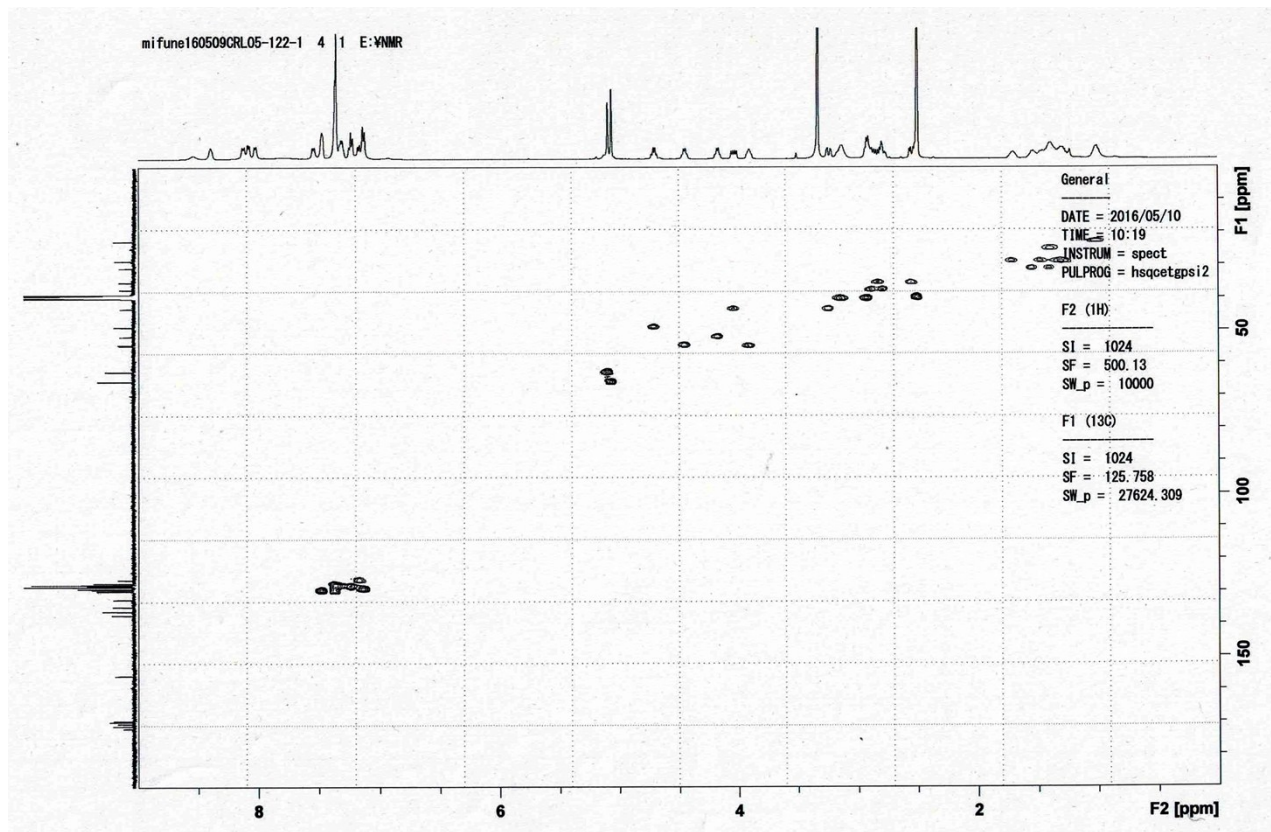
cyclic pentapeptide 24



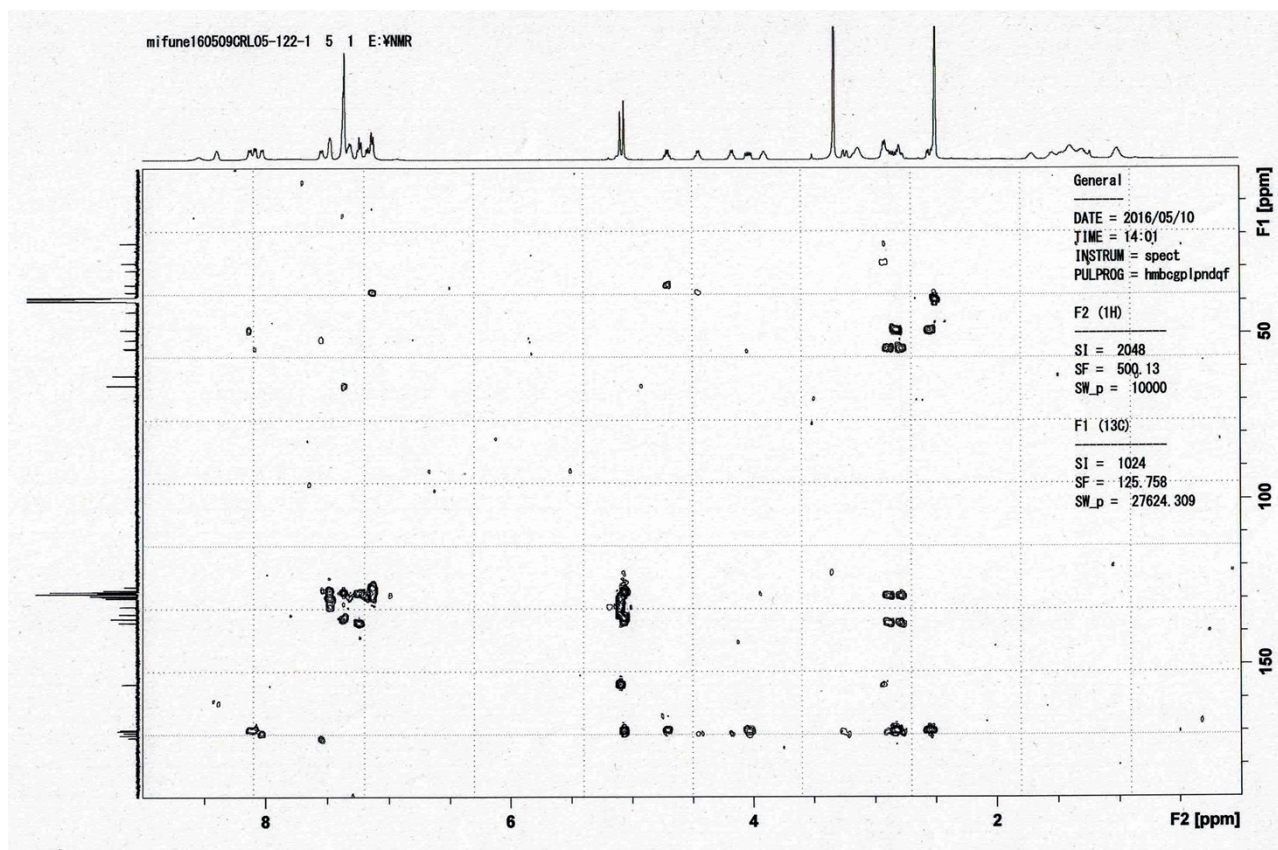
(¹H-¹H COSY)



(HSQC)



(HMBC)



cyclic RGD peptide (25)

