

# 水中におけるプロリン残基を含むジケトピペラジンの コンホメーション変化とエピメリ化

石津 隆、堤 広之、横山 えみ、川本 晴香、横田 留奈

*Chem. Pharm. Bull.*, **65**(6), 598-602 (2017)

## Conformation Change and Epimerization of Diketopiperazines Containing Proline Residue in Water

Takashi Ishizu, Hiroyuki Tsutsumi, Emi Yokoyama, Haruka Kawamoto,  
Runa Yokota

**ABSTRACT:** In water, diketopiperazines cyclo(L-Pro-L-Xxx) and cyclo(L-Pro-D-Xxx) (Xxx=Phe, Tyr) formed an intramolecular hydrophobic interaction between the main skeleton part and their benzene ring, and both cyclo(L-Pro-L-Xxx) and cyclo(L-Pro-D-Xxx) took a folded conformation. The conformational changes from folded to extended conformation by addition of several deuterated organic solvents (acetone- $d_6$ , metanol- $d_4$ , dimethyl sulfoxide- $d_6$  (DMSO- $d_6$ )) and the temperature rise were investigated using  $^1\text{H-NMR}$  spectra. The results suggested that the intramolecular hydrophobic interaction of cyclo(L-Pro-D-Xxx) formed more strongly than that of cyclo(L-Pro-L-Xxx). Under a basic condition of  $1.0 \times 10^{-1}$  mol/L potassium deuteroxide, enolization of  $\text{O}_1\text{-C}_1\text{-C}_9\text{-H}_9$  moiety of cyclo(L-Pro-L-Xxx) occurred, while that of the  $\text{O}_4\text{-C}_4\text{-C}_3\text{-H}_3$  moiety did not. Cyclo(L-Pro-L-Xxx) epimerized to cyclo(D-Pro-L-Xxx), while cyclo(L-Pro-D-Xxx) did not change.

抄録 水中において、ジケトピペラジン cyclo(L-Pro-L-Xxx) と cyclo(L-Pro-D-Xxx) (Xxx=Phe, Tyr) は主骨格部分とベンゼン環の間で分子内疎水性相互作用を形成し、cyclo(L-Pro-D-Xxx) と cyclo(L-Pro-D-Xxx) は互いに折り畳み構造をとっていた。そこで重有機溶媒 (acetone- $d_6$ , metanol- $d_4$ , dimethyl sulfoxide- $d_6$  (DMSO- $d_6$ )) の添加と温度上昇による折り畳みから伸長構造へのコンホメーション変化は  $^1\text{H-NMR}$  を用いて調べられた。その結果、cyclo(L-Pro-D-Xxx) の分子内疎水性相互作用は、cyclo(L-Pro-D-Xxx) よりも強く形成されていることが明らかになった。また、 $1.0 \times 10^{-1}$  mol/L 重水酸化カリウム存在下、cyclo(L-Pro-D-Xxx) の  $\text{O}_1\text{-C}_1\text{-C}_9\text{-H}_9$  部位ではエノール化が起こったが、 $\text{O}_4\text{-C}_4\text{-C}_3\text{-H}_3$  部位では起こらなかった。さらに、cyclo(L-Pro-D-Xxx) から cyclo(L-Pro-D-Xxx) へのエピメリ化は起こったが、cyclo(L-Pro-D-Xxx) では起こらなかった。