

## N-メチル-N,N'-ジフェニルスクアルアミドの溶媒依存的立体転換

(お茶大院理<sup>1</sup>・医科歯科大生材研<sup>2</sup>・甲南大理工<sup>3</sup>・昭和薬科大<sup>4</sup>) ○田中 希実子<sup>1</sup>・  
神田 翠<sup>1</sup>・藤井 晋也<sup>2</sup>・片桐 幸輔<sup>3</sup>・川幡 正俊<sup>4</sup>・影近 弘之<sup>2</sup>・棚谷 綾<sup>1</sup>

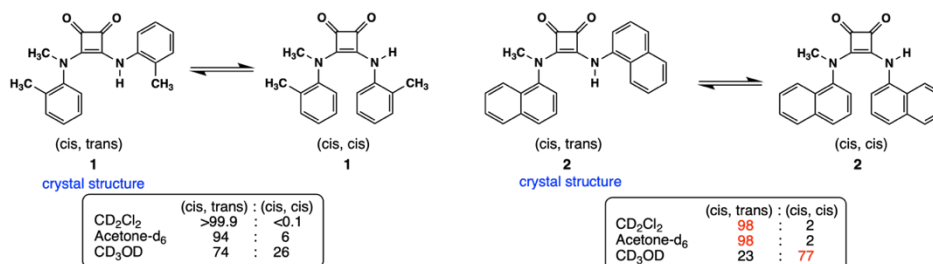
Solvent-dependent conformational alteration of *N*-methyl-*N,N'*-diphenylsquaramides  
(<sup>1</sup>*Department of Chemistry, Faculty of Science, Ochanomizu University*; <sup>2</sup>*Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University*; <sup>3</sup>*Department of Chemistry of Functional Molecules, Faculty of Science and Engineering, Konan University*; <sup>4</sup>*Faculty of Pharmaceutical Science, Showa Pharmaceutical University*) ○Kimiko Tanaka<sup>1</sup>,  
Midori Kanda<sup>1</sup>, Shinya Fujii<sup>2</sup>, Kosuke Katagiri<sup>3</sup>, Masatoshi Kawahata<sup>4</sup>, Hiroyuki Kagechika<sup>2</sup>,  
Aya Tanatani<sup>1</sup>.

Squaramide is a diamino derivative of squaric acid, a four-membered cyclic dibasic acid. *N,N'*-Dimethylation of *N,N'*-diphenylsquaramide changed the conformation from (trans, trans) to (cis, cis) form. Previously, we found *N*-methyl-*N,N'*-diphenylsquaramide such as compound **1** showed solvent-dependent change of the conformational ratio. In this study, to clarify the origin of solvent-dependent conformational switching, we synthesized *N*-methyl-*N,N'*-diphenylsquaramide derivatives, having various substituents on the phenyl rings. As a result, *N*-monomethyl derivatives had (cis, trans) form in the crystal, independent on the recrystallization solvent, and most derivatives showed the solvent-dependent change of the conformational ratio. Among them, the naphthyl derivative **2** showed remarkable solvent-dependency, and existed predominantly (cis, trans) form (98%) in CD<sub>2</sub>Cl<sub>2</sub> or acetone-*d*<sub>6</sub>, whereas the (cis, cis) form was major (77%) in CD<sub>3</sub>OD. These results indicated that squaramides could be applied to development of solvent-responsive molecular switch.

**Keywords** : Squaramide; Solvent-dependent conformational switching; Cis-trans isomer.

スクアルアミドは、四員環骨格を有するスクアリン酸のジアミノ誘導体である。一般に、*N,N'*-ジフェニルスクアルアミドは、結晶、溶液中で(trans, trans)型で存在するが、*N,N'*-ジメチル化により、芳香環が近接して向かい合う(cis, cis)型へ立体転換する<sup>1,2)</sup>。演者らは、芳香族スクアルアミドの立体構造解析の過程で、*N*-メチル-*N,N'*-ジフェニルスクアルアミド **1** が、溶媒依存的に(cis, trans)型と(cis, cis)型のコンフォメーション比を変化させることを見いだした。本研究では、その構造要求性を明らかにするために、芳香環上に種々の置換基をもつ誘導体を系統的に合成し、立体構造を解析した。

X線結晶構造解析より、多くの誘導体が、結晶中、再結晶溶媒によらず(cis, trans)型をとることがわかった。一方、ナフチル体 **2** が顕著な溶媒依存性を示し、CD<sub>2</sub>Cl<sub>2</sub>、Acetone-*d*<sub>6</sub> 中では(cis, trans)型で存在するのに対して、CD<sub>3</sub>OD 中では(cis, cis)型を優先させ、溶媒によって主コンフォマーが逆転した。



1) Muthyala, R. S. et al. *Org. Lett.* **2004**, 6, 4663; 2) Arimura, M. et al. *ChemPlusChem* **2021**, 86, 198.