Epimerization of á-amino Nitriles to Single Stereoisomers in the Solid State

Akira Uchida[a], Rumiko Sakurai[b], Tetsutaro Hattori[b], Masanori Yamaura[c], [a]*Toho University.* [b]*Tohoku University.* [c]*Iwaki Meisei University*. E-mail: auchida@biomol.sci.toho-u.ac.jp

Enantiomeric or diastereomeric enrichment to a single isomer has had only limited success to date. We have found that a diastereomeric mixture of α-amino nitriles, which was prepared by the diastereoselective Strecker reaction using the amino alcohol as a chiral auxiliary, thermally epimerizes to a single stereoisomer in the solid state. X-ray structure analyses have shown that the α-amino nitrile, [1*S*,2*R*,(*SR*)]-N-cyano(phenyl)methyl-1-aminoindan-2-ol, epimerizes at 65 °C to give a single diastereomer with an (*S*)-configureation ((*S*)-isomer) at the α position to the nitrile moiety. Namely the (*R*)-isomer is thermally unstable and the (*S*)-isomer is stable in the solid state. In DMSO solution, the diastereomerically pure (*S*)-isomer epimerizes at room temperature to give a 1 : 1 mixture of the (*S*)- and (*R*)-isomers. Therefore the cause of thermal unstability of (*R*)-isomer in the solid state should be ascribed to the crystal structure. In the (*R*)-isomer crystal there are two hydrogen bonds, an intramolecular N-H…O and an intermolecular CN…HO bonds which promote dissociation of the cyanide anion. On the other hand, the intramolecular O-H...N bond in the (*S*)-isomer crystal retards the dissociation of the cyanide anion. As a result, the (*R*)-isomer selectively epimerizes to the (*S*)-counterpart via an iminium or imine intermediate.

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