Novel Applications of Tetrazoles Derived from the TMSN3-Ugi Reaction

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Stellingen

Behorende bij het proefschrift:

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1. Multicomponent reactions are very fruitful in accessing various drug-like scaffolds, for example, tetrazoles (this thesis).

2. A concise and rapid synthetic route to α-amino acid bioisosteric α-amino tetrazoles is developed by using a key azido-Ugi reaction, exemplified in the synthesis of all 20 natural proteinogenic amino acids and 4 others (Chapter 3).

3. Tritylamine as a convenient and easily cleavable ammonia surrogate reacts together with aldehydes, TMS-azide, and isocyanides to yield *N*-trityl α-aminotetrazoles under very mild conditions (Chapter 4).

4. A fast and reliable synthetic route to 5- and 6-membered unsubstituted tetrazololactams is established, using a key azido-Ugi reaction followed by a deprotection and cyclisation step (Chapter 5).

5. A tight coordination with the binuclear Mn (II) center at the active site of human arginase is required to mimic the tetrahedral intermediate formed by the nucleophilic hydroxide ion attack onto the guanidinium carbon during the arginine hydrolysis process (Chapter 6).

6. A potent human arginase inhibitor should contain proper substituted groups which can recognize the hydrogen bond network composed of amino acid residues at the mouth site of human arginase (Chapters 6 - 7).

7. A nonclassical bioisosteric replacement of carboxyl group with tetrazolyl moiety at α position of 2-amino-6-boronohexanoic acid (ABH) results in novel human arginase inhibitors that are successfully synthesized via multicomponent reaction (Chapter 7).

8. A single hand that wipes tears during failures is of much higher value than countless hands that come together to clap on success (锦上添花易，雪中送炭难).

9. Each man/woman is the architect of his/her own fate (命运掌握在自己手里).