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Synthesis of azetidines and pyrrolidines: Towards medicinal chemistry and organocatalysis applications

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Room temperature iodocyclisation of homoallylamines stereoselectively delivers functionalised 2- (iodomethyl)azetidine derivatives in high yield. Increasing reaction temperature from 20°C to 50°C switches the reaction outcome to realise the stereoselective formation of functionalised 3-iodopyrrolidine derivatives. It was shown that these pyrrolidines are formed via thermal isomerisation of the aforementioned azetidines. Primary and secondary amines could be reacted with iodomethyl azetidine derivatives to deliver stable methylamino azetidine derivatives. With subtle changes to the reaction sequences homoallyl amines could be stereoselectively converted to either cis- or trans- substituted 3-amino pyrrolidine derivatives at will. The stereochemical divergent synthesis of cis and trans substituted pyrrolidines supports an ion part, aziridinium, isomerisation pathway for azetidine to pyrrolidine isomerisation. Six azetidine derivative were probed in a zebrafish embryo developmental assay for capacity to illicit morphological changes. The range of effects across the probed molecules demonstrates the suitability of this assay for screening azetidine derivatives. One of the probed molecules, exhibited particularly promising effects in the developmental assay.

Biography

Antonio Feula is a PhD Chemist with 10 years of research experience in organic multi-step synthesis, drug discovery, surface chemistry, medicinal and supramolecular chemistry. Expertise ranges from multi-step synthesis (designing and performing) to chromatography (sample isolation, purification) and NMR methodologies. He has been part of several cross-functional teams including engineers, chemists and biologists. Antonio was a post-doctoral research fellow at the University of Reading and Oxford before moving to USA where he worked for Merck, Coty and Orthobond. He is currently involved in the drug discovery of small molecules for genetic heart diseases at Myokardia in South San Francisco.

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