Biotransformation of bicyclic amides by *Cunninghamella elegans*

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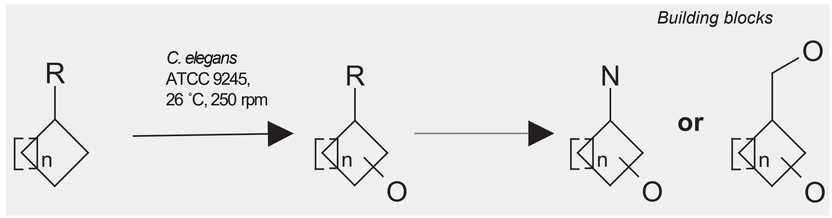
Introduction and Aim

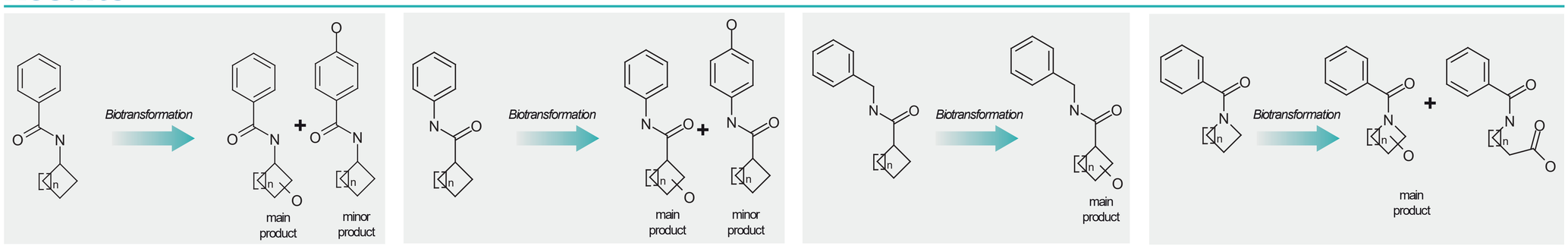
Of particular interest is the use of microorganisms like fungi from the genus Cunninghamella, recognized for their ability to biotransformation a wide range of organic compounds1. The products of biotransformation can be utilized to create new molecules. In the past decade, research has demonstrated that various saturated (azo)cyclic compounds can imitate the central phenyl ring found in bioactive compounds, potentially enhancing their physicochemical properties2,3. Developing biocatalytic methods to modify saturated cyclic, bicyclic, and spiro compounds could provide new building blocks for drug development. Our current work examines the biotransformation potential of *Cunninghamella elegans* ATCC 9245 for regio- and stereoselective hydroxylation of these bioisosteric scaffolds. For this purpose, we utilized different derivatives of (azo)cycloalkanes, including bicyclic and spiro compounds. In general, we explored several homologous series of bicyclic amides: N-cycloalkylbenzamides, N-phenylcycloalkanbenzamides, N-phenylcycloalkancarboxamides , and 1-benzyl-azocycloalkanes.

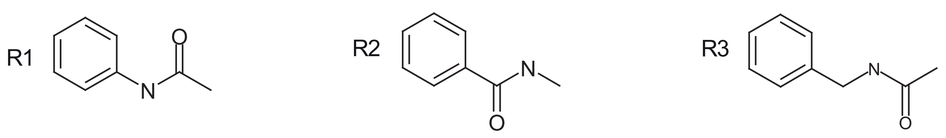


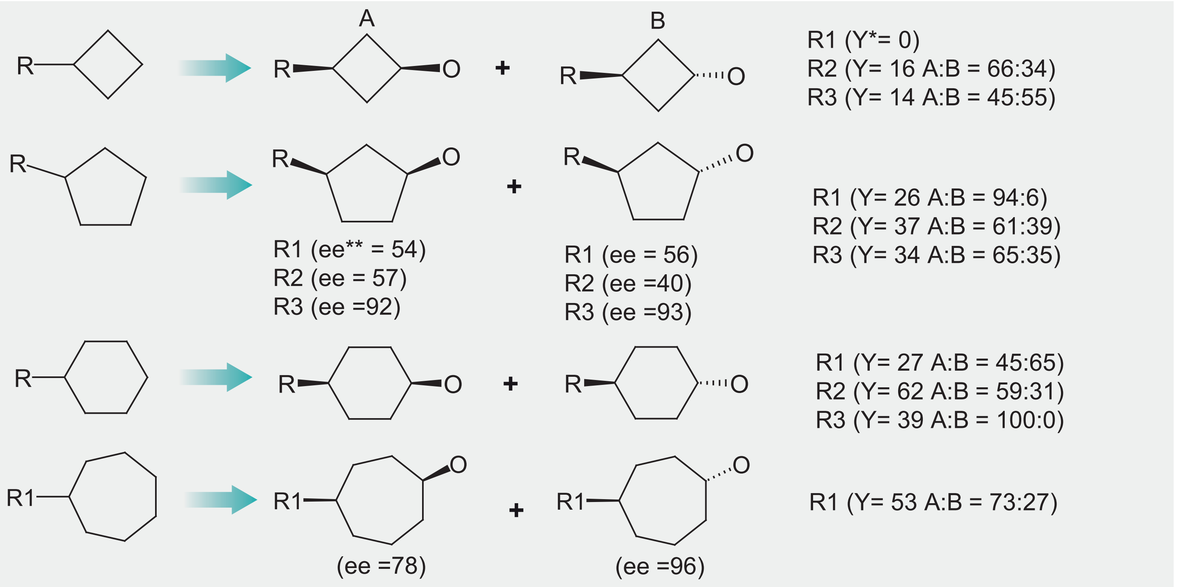
Methods

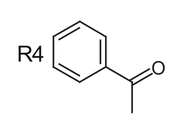
Strain of C. elegans ATCC 9245 was used for the biotransformation of the studied compounds. The submerged culture was grown on Sabouraud dextrose agar (26 ˚C, 250 rpm) for 3 days before addition of compounds. All compounds were added to the fungal culture at a final concentration of 0.2 g/l. The biotransformation time was 72 hours. Metabolites were extracted by ethyl acetate and assessed by HPLC-MS, purified using preparative reversed phase HPLC. The structures of metabolites were approved by 1H, 13C NMR. Stereoselectivity of biotransformation process was evaluated by chiral HPLC.

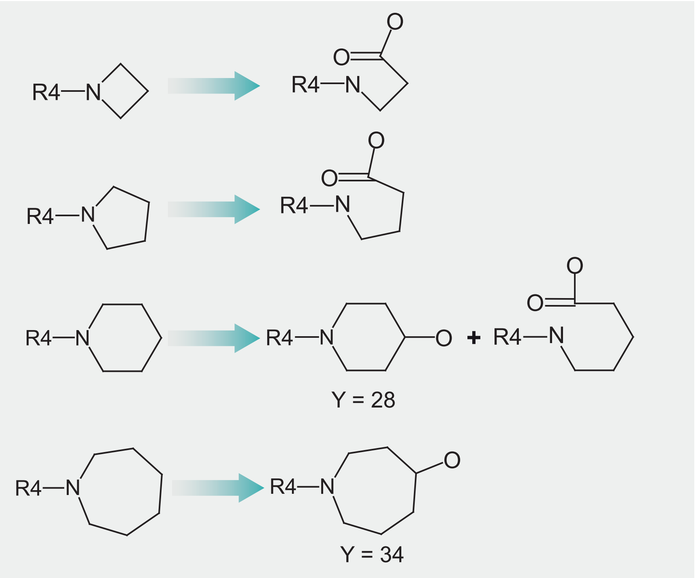
Results



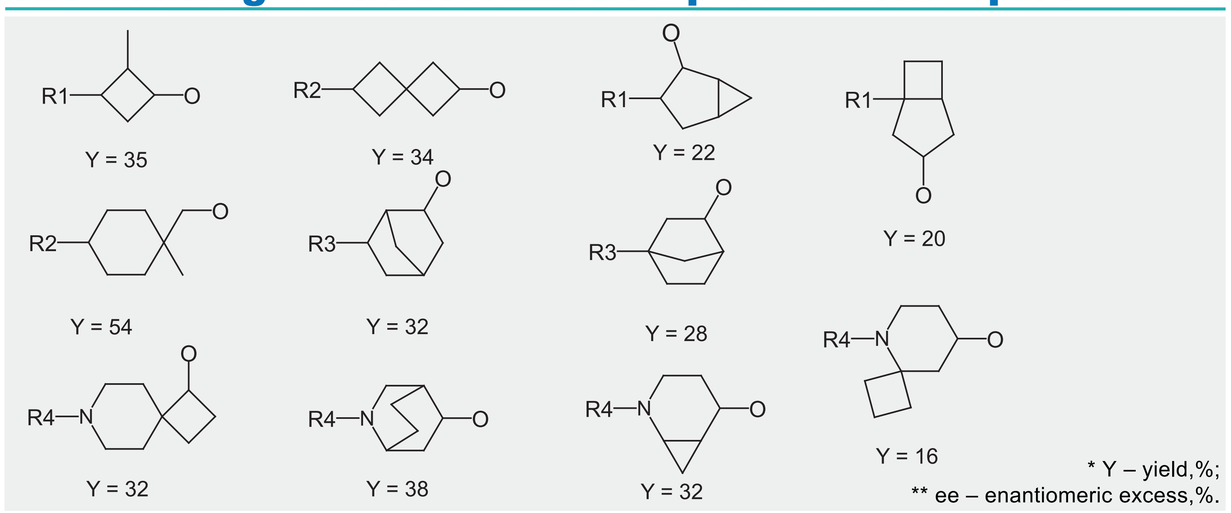




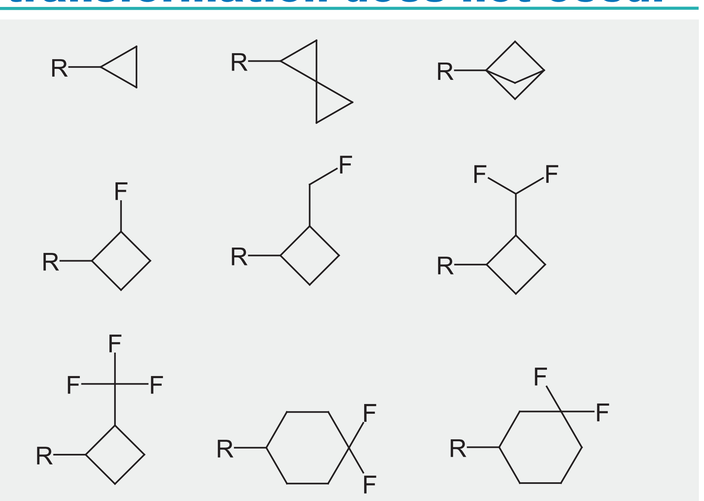




Showcasing biotransformation product examples



Biotransformation does not occur



Conclusions

The results indicated that the hydroxylation of the examined compounds primarily occurs at the aliphatic ring (with some exceptions) and predominantly at the para position. This allows the derivatives studied to be used for producing modified cyclic building blocks.

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References

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