DEVELOPING A 'REVERSE-BIOMIMETIC' SYNTHESIS OF AROGENATE AND ITS ANALOGUES

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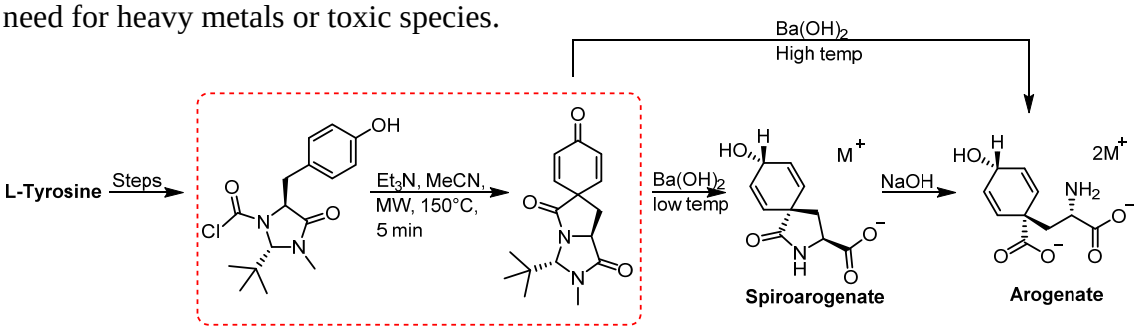
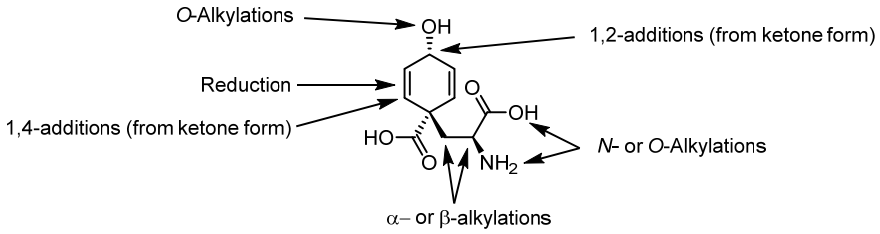
Arogenate is a key intermediate in the shikimate biosynthetic pathway to aromatic amino acids tyrosine and phenylalanine. Only two syntheses of arogenate have been reported, neither of which exploit the obvious starting material, L-tyrosine itself.[1],[2] Uniquely, our work focuses on a 'reverse-biomimetic' synthesis of arogenate starting from this inexpensive, enantiopure amino acid. Interestingly, the synthetic route proceeds via a novel and mechanistically unusual dearomatising spirocyclisation reaction. This intramolecular acylation, which utilises a carbamoyl chloride tether to produce a spirocyclic lactam, can be performed using low-cost reagents and without the need for heavy metals or toxic species.



Scheme 1: Overview of the synthetic concept.

The biosynthetic pathways to aromatic amino acids are present in plants, bacteria and fungi but completely absent in animals.[3] Targeting the enzymes involved in this pathway with synthetic analogues of arogenate could enable the development of new, safe and selective herbicides and antibiotics.



Scheme 2: Derivatisation of arogenate for agrochemical studies.

[1] Crossley, M. J.; Reid, R. C. *J. Chem. Soc. Chem. Commun.* **1994**, 2237.

[2] Danishefsky, S.; Morris, J.; Clizbe, L. A. *J. Am. Chem. Soc.* **1981**, *103*, 1602.

[3] Maeda, H.; Dudareva, N. *Annu. Rev. Plant Biol.* **2012**, *63*, 73.