Enantioselective Construction of Complex Spirocyclic Derivatives

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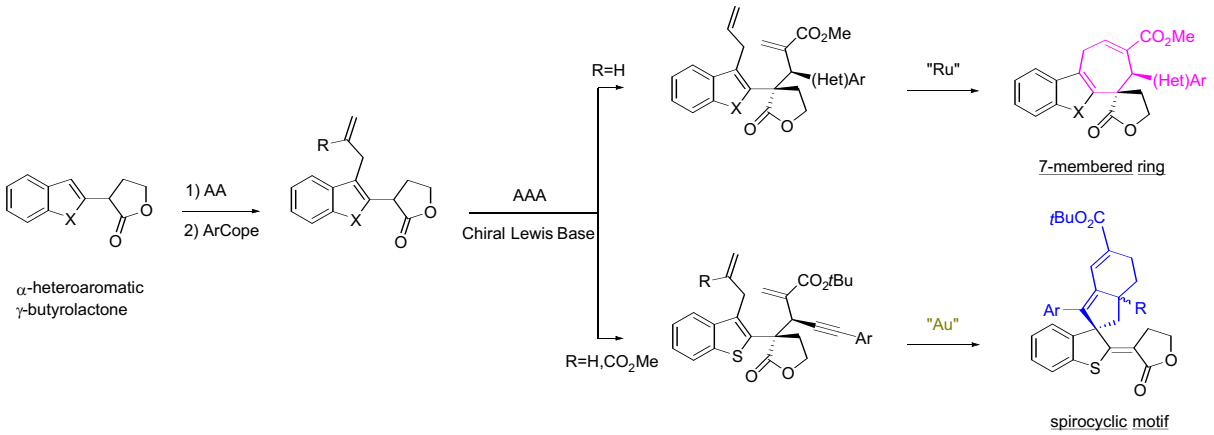
One of the great challenge of organic chemists is to form carbon-carbon bonds leading to the creation of a stereogenic center in a controlled manner. This type of transformation enables the construction of three-dimensional structures and thus provide useful tools and methods for the synthesis of biologically active molecules.[1] This exploitation of space is at the heart of the latest studies carried out by our laboratory. One of our recent objectives is to develop the synthesis of 2 families of chiral heteroaromatic molecules bearing a spirocyclic motif from a common precursor, an α-heteroaromatic-γ-butyrolactone.

The envisaged strategies involve 4 steps, with the first three being the same for both synthesis. The allyl group on the heteroaromatic ring was introduced through a sequence involving an allylic alkylation (AA) reaction followed by an aromatic Cope rearrangement,[2,3] while the chiral chain containing the α,β unsaturated ester was introduced through an organocatalyzed asymmetric allylic alkylation (AAA) of the lactone.[4] The formation of the 7-membered ring was achieved through a ring-closing metathesis reaction involving an electron-rich and an electron-poor alkene, while the spirocyclic motif was formed under gold catalysis.



References

[1] Humblet, C. et al. *J. Med. Chem.* **2009**, *52*, 6752-6756.
[2] Greening, A. J. et al. *Org. Biomol. Chem.* **2021**, *19*, 2385-2398.
[3] Riguet, E. et al. *Chem. – Eur. J.* **2024**, *30*, e202304138.
[4] Riguet, E. et al. *Org. Lett*. **2022**, *24*, 5351-5355.