

## Enantioselective Synthesis of Biaryl Atropisomers by Dynamic Kinetic Resolution

**Specific Aim:** This proposal aims to develop an asymmetric method for the synthesis of biaryl atropisomers with chiral reagents or catalysts. The key innovation will be the use of configurationally stable biaryl phenols, which will be oxidized to the configurationally unstable quinone methides, for a dynamic kinetic resolution leading to enantiomerically enriched products.

**Background and Significance.** *Atropisomerism* is the axial chirality arising from restricted rotation about a single bond. The ability of axial chirality to exert a profound influence on the shape, structure, and reactivity of organic molecules has found widespread application throughout the spectrum of organic chemistry, including widely used classes of *ligands for asymmetric synthesis, bioactive natural products, molecular machines, and stereoselective synthesis.*

In contrast to parallel developments for the synthesis of carbon-centered chirality, where asymmetric synthesis has rendered optical resolution almost obsolete, enantiomerically pure atropisomers are most often prepared by separation of diastereomeric derivatives. Although notable progress has been made recently through the use of stoichiometric quantities of chiral reagents and tethers, the interest in atropisomerically pure molecules currently outpaces the development of methods for their synthesis. Novel methods for the formation of enantiomerically pure axial chirality represent a frontier in organic synthesis.

**Proposed Work.** In order to address the need for a general method for the preparation and manipulation of enantiomerically pure atropisomers, a new concept for their dynamic, kinetic resolution is proposed. The proposed reactions consists of four key steps:

- The generation of a *quinone methide* **2** from a racemic mixture of biaryl phenol **1**.
- The ability of the quinone methide **2** to *rotate about the biaryl bond* due to a lower barrier of rotation.
- The *diastereoselective complexation* of the quinone methide to a chiral Lewis acid.
- The *trapping* of quinone methide-Lewis acid complex **3** by a nucleophile to regenerate biaryl phenol **4** enriched in one atropisomer.

