

Asymmetric Synthesis of Spiroisoxazolines and Spirooxazines via Chiral Hypoiodite-catalyzed Enantioselective Oxidative Dearomatization of Arenols

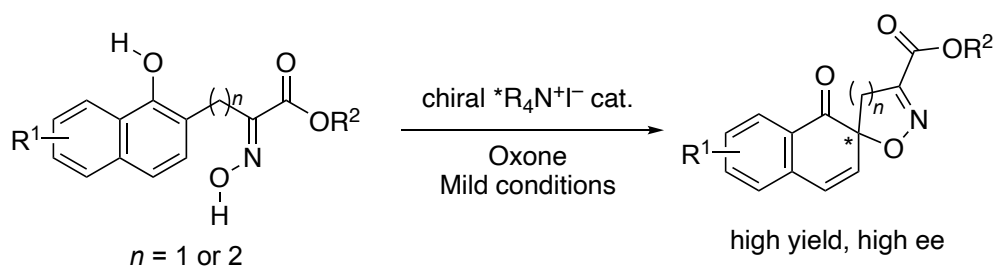
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Optically active spiroisoxazolines and spirooxazines are important molecular scaffolds found in various natural products and biologically active substances.¹

We have developed enantioselective oxidative dearomative coupling reactions of arenols catalyzed by chiral quaternary ammonium hypoiodite species,² generated *in situ* via the oxidation of corresponding iodides with suitable oxidants such as hydrogen peroxide and oxone.³ Compared to the conventional methods using transition-metal catalysts or hypervalent iodine reagents, this oxidation system is environmentally benign and operates under mild reaction conditions, producing only water or inorganic salts as byproducts. However, the enantioselective reactions developed to date have been limited to the spirocyclization of arenols bearing carboxylic acids as internal nucleophiles.³

Our findings suggest that the Brønsted acidity of the internal nucleophile in the substrate (e.g., carboxylic acids) is critical for achieving high asymmetric induction in these oxidative dearomatization reactions. Therefore, we hypothesized that α -acyl oximes, which exhibit acidity comparable to carboxylic acids, would be suitable substrates for this enantioselective oxidation system. Herein, we report the enantioselective oxidative dearomative spirocyclization of hydroxyaryl oximes catalyzed by chiral ammonium hypoiodite. This work represents the first catalytic enantioselective synthesis of spiroisoxazolines and spirooxazines, achieved with high yield and high enantioselectivity.



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