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Synthesis of new, cell permeable, esterase hydrolyzable analogues of alpha-ketoglutarate, alpha-ketoglutaramate and succinyl phosphonate: tools for the study of cellular function

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Abstract

The α -ketoglutarate dehydrogenase complex (KGDHC) is a control point of tricarboxylic acid (TCA) cycle. Previous studies have shown that many neurodegenerative diseases are related to the activity of brain KGDHC. To study the specific mechanism of KGDHC and its involvement requires potent and specific inhibitors as probes. Dr. Denton's group has synthesized some analogs of α -ketoglutarate and shown some of them have good cell permeability and can be hydrolyzed by the esterases in the cell. This presentation will focus on how to use chemistry methods to synthesize KGDHC inhibitors and how to use NMR spectroscopy confirm the results.