Chemoenzymatic Synthesis Of Neuroexcitatory And Cuaac-Compatible Kainoid Aalogs

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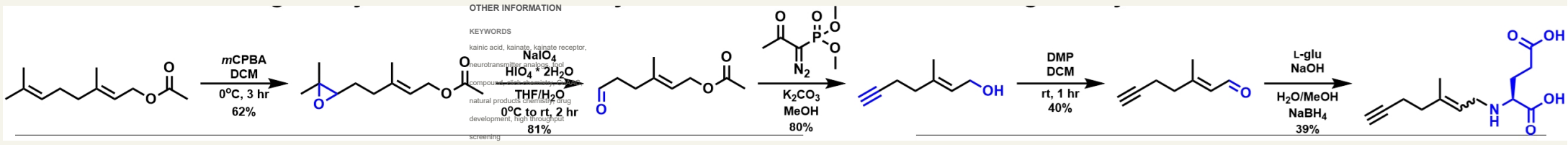
BACKGROUND

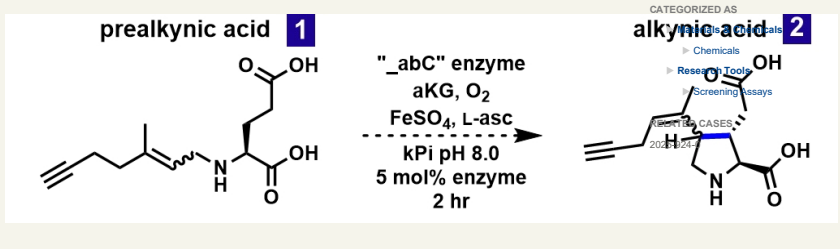
Kainate receptors, also known as kainic acid receptors are ionotropic receptors that bind to and are responsive to glutamate in neurons. These were originally identified as being activated by the compund kainic acid, orignally isolated from algae. Postsynaptic kainate receptors are involved in excitatory neurotransmission while presynaptic kainate receptors are involved in inhibitory neurotransmission. Kainic acid is a potentially very useful compound but very difficult to synthesize. As a result, there are very few pharmacological tool compounds to study kainate receptors and none that are readily tunable to install labeling compounds.

TECHNOLOGY DESCRIPTION

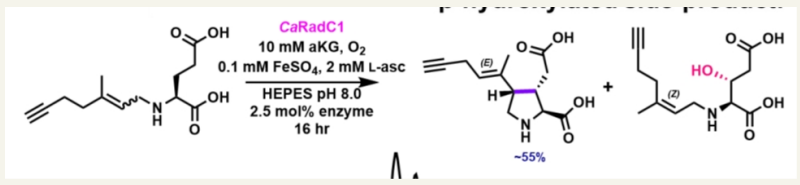
Researchers in Shaun McKinnie's lab at UC Santa Cruz have developed a chemoenzymatic route to produce not only kainic acid, but also "clickable" kainic acid derivatives to which fluorescent and other labels can be readily attached.



Then the RadC1 enzyme from the red algae Chondria armata cyclizes prealkynic acid into alkynic acid



Then further optimization and scale up yields a kainoid ring and a β-hydroxylated side product



With this structure, Copper catalyzed azide-alkyne cycloaddition (CuAAC) or "click" chemistry allows rapid diversification from the alkynic scaffold and in vivo functionalization with bioorthogonal handles.

APPLICATIONS

- Tool compound for study of kainoid receptor
- Drug development for new kainoid receptor agonists
- High throughput screening of new candidate kainoid receptor agonists

ADVANTAGES

- Facile synthesis
- Addition of labels by click chemistry
- Labels don't affaect kainic acid binding

INTELLECTUAL PROPERTY INFORMATION

Patent Pending

RELATED MATERIALS

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OTHER INFORMATION

KEYWORDS

kainic acid, kainate, kainate receptor, neurotransmitter analogs, tool compound, click chemistry, CuAAC, natural products chemistry, drug development, high throughput screening

CATEGORIZED AS

- Biologics & Chemicals
- Chemicals
- Research Tools
- Screening Assays

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