

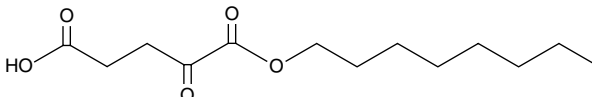
Product Information



Octyl- α -ketoglutarate

Item No. 11970

CAS Registry No.: 876150-14-0
Formal Name: 2-oxo-1-octyl ester-pentanedioic acid
Synonym: α -KG octyl ester
MF: $C_{13}H_{22}O_5$
FW: 258.3
Purity: $\geq 95\%$
Stability: ≥ 1 year at -20°C
Supplied as: A solution in methyl acetate



Laboratory Procedures

For long term storage, we suggest that octyl- α -ketoglutarate be stored as supplied at -20°C . It should be stable for at least one year.

Octyl- α -ketoglutarate is supplied as a solution in methyl acetate. To change the solvent, simply evaporate the methyl acetate under a gentle stream of nitrogen and immediately add the solvent of choice. Solvents such as ethanol, DMSO, and dimethyl formamide (DMF) purged with an inert gas can be used. The solubility of octyl- α -ketoglutarate in ethanol is approximately 20 mg/ml and approximately 10 mg/ml in DMSO and DMF.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. If an organic solvent-free solution of octyl- α -ketoglutarate is needed, it can be prepared by evaporating the methyl acetate and directly dissolving the neat oil in aqueous buffers. The solubility of octyl- α -ketoglutarate in PBS, pH 7.2, is approximately 1 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Hypoxia-inducible factor 1 α (HIF-1 α) turnover is initiated by prolyl hydroxylases (PHD), which hydroxylate proline residues on HIF-1 α , facilitating ubiquitination. PHD activity is linked to the tricarboxylic acid (TCA) cycle, since the intermediate α -ketoglutarate is a PHD substrate and succinate and fumarate inhibit PHD. Mutations in enzymes associated with the TCA cycle occur in certain cancers.¹ Octyl- α -ketoglutarate is a stable, cell-permeable form of α -ketoglutarate, which accumulates rapidly and preferentially in cells with a dysfunctional TCA cycle.² When used at 1 mM, it stimulates PHD activity, increasing HIF-1 α turnover.^{2,3} In addition, Octyl- α -ketoglutarate competitively blocks succinate- or fumarate-mediated inhibition of PHD.²

References

1. Gottlieb, E. and Tomlinson, I.P.M. Mitochondrial tumour suppressors: A genetic and biochemical update. *Nat. Rev. Cancer* **5**, 857-866 (2005).
2. MacKenzie, E.D., Selak, M.A., Tennant, D.A., *et al.* Cell-permeating α -ketoglutarate derivatives alleviate pseudohypoxia in succinate dehydrogenase-deficient cells. *Mol. Cell. Biol.* **27**(9), 3282-3289 (2007).
3. Zhao, S., Lin, Y., Xu, W., *et al.* Glioma-derived mutations in IDH1 dominantly inhibit IDH1 catalytic activity and induce HIF-1 α . *Science* **324**(5924), 261-265 (2009).

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