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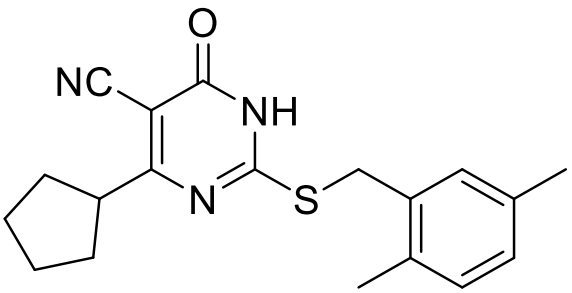
# Technical Information about HJC0197

**Membrane-permeant inhibitor of Epac 1 and Epac 2**

Update: December 4, 2017 AI




**Abbreviation:** **HJC0197**

| Formula | CAS No. | Molecular Weight | UV | BIOLOG Cat. No. |
|---|---|---|---|---|
| $C_{19}H_{21}N_3OS$ | [1383539-73-8] | 339.5 | $\lambda_{max}$ 304 nm / ε 14700 / pH 7 | C 136 |

**Name:** 4- Cyclopentyl- 2- (2, 5- dimethylbenzylsulfanyl)- 6- oxo- 1, 6- dihydropyrimidine- 5- carbonitrile

**Description / Properties:** According to Chen et al. (2012) HJC0197 is a membrane-permeant inhibitor of both exchange proteins activated directly by cyclic AMP, Epac 1 and Epac 2. HJC0197 displays an *in vitro* $IC_{50}$ value of 5.9 µM for Epac 2 in competing with 8-NBD-cAMP (our Cat. No. N 002) binding. It displays sufficient selectivity for Epac proteins compared to cyclic AMP-dependent protein kinase I and II at 25 µM concentration in *in vitro* assays. Pretreatment with 10 µM HJC0197 inhibits Epac 1 and Epac 2 activation with 10 µM 8-pCPT-2'-O-Me-cAMP-AM (our Cat. No. C 051) in intact cells (Chen et al. 2012).
In a recent report it was suggested that general protein denaturing properties are the molecular basis for the inhibitory action of HJC0197, thus raising concerns about the selectivities for Epac 1 and Epac 2 (Rehmann 2013).

**Specification:** Crystallized or lyophilized solid. **Please keep in mind that equal concentrations of the compound may look different in volume due to sensitivity of the lyophilized form to humidity. The compound can even contract to small droplets.** Normally the product is located in the conical bottom of the tube. Micromolar quantities are determined by weight.

**Purity:** Typical analysis is better than 95% (HPLC / UV / 270 nm). The product is not sterile and has not been tested for endotoxins.

**Stability and Storage:** HJC0197 is chemically rather stable and does not need special care during handling or shipment. Nevertheless, we recommend that the compound should be stored in the freezer (-20° Celsius necessary, -80° recommended), for longer storage periods preferably in freeze-dried form.

**Toxicity and Safety:** Please keep in mind, that the *in vivo* properties of this compound are not sufficiently characterized up to now. Avoid skin contact or ingestion and allow only trained personnel to handle the product.
Our products are designed, developed and sold for research purposes only! They are intended for *in vitro* and nonhuman *in vivo* laboratory applications. Any other use requires approval of health authorities.
**Not for drug, household or related uses!**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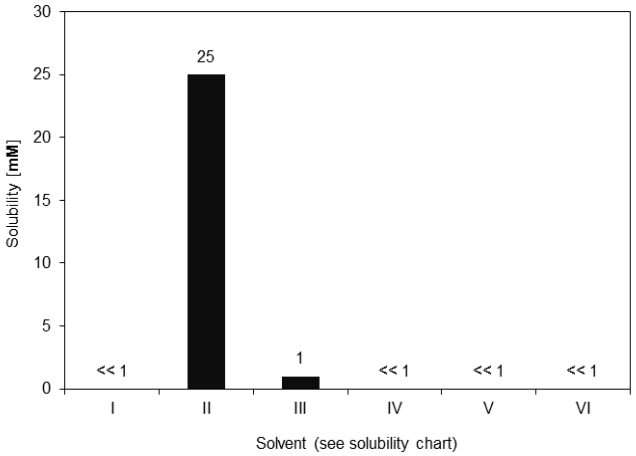
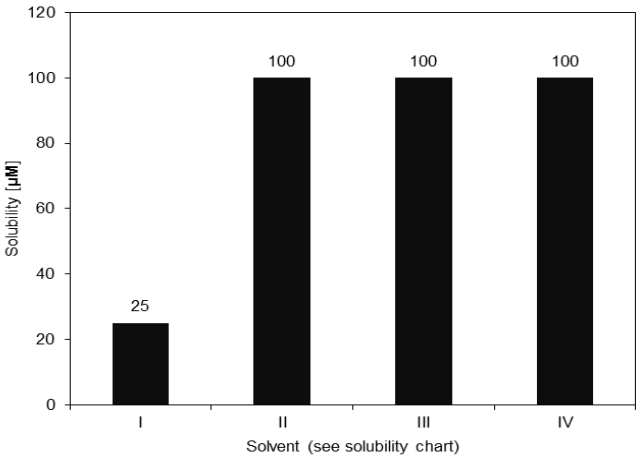
**Solubility:** Detailed information on the solubility of HJC0197 in water and various buffers are listed in the solubility chart below. Concentrations have been determined at ambient temperature and can be considered as concentrations usually obtainable, however, slight batch-to-batch variations cannot be ruled out.

| No. | Solvent | Solubility [mM] |
|---|---|---|
| I | $H_2O$ | << 1 |
| II | DMSO | 25 |
| III | Ethanol 96% | 1 |
| IV | PBS, pH 7.4 | << 1 |
| V | 25 mM Hepes/NaOH, pH 7.2 | << 1 |
| VI | 25 mM Tris/HCl, pH 7.4 | << 1 |




Due to its rather high lipophilicity, the solubility of HJC0197 in water or buffers is limited. We suggest to first use a small amount of DMSO for dissolution, and to dilute with DMSO and water or buffer down to the final concentration to be used in the biological assay (see below for corresponding protocols). Please rinse tube walls carefully and preferably use ultrasonic or vortex to achieve total and uniform mixing. When opening the tube please make sure that no substance is lost within the cap.

| No. | Solvent | Solubility [µM] |
|---|---|---|
| I | $H_2O$ (1% DMSO) | 25 |
| II | PBS, pH 7.4 (1% DMSO) | 100 |
| III | 25 mM Hepes/NaOH, pH 7.2 (1% DMSO) | 100 |
| IV | 25 mM Tris/HCl, pH 7.4 (1% DMSO) | 100 |




Preparation of a 25 µM solution in water (1% DMSO):

Add 200 µL DMSO to a 5 µmol vial of HJC0197 to achieve a 25 mM solution. Use 10 µL of this solution and dilute with 90 µL DMSO to get a 2.5 mM solution. Addition of 990 µL water to 10 µL of this 2.5 mM DMSO solution will result in a 25 µM solution in water (1% DMSO).

Preparation of a 100 µM solution in various buffers (1% DMSO):

Add 200 µL DMSO to a 5 µmol vial of HJC0197 to achieve a 25 mM solution. Use 40 µL of this solution and dilute with 60 µL DMSO to get a 10 mM solution. Addition of 990 µL buffer (PBS, Hepes, Tris) to 10 µL of this 10 mM DMSO solution will result in a 100 µM solution in buffer (1% DMSO).

## Selected References for HJC0197:

Parnell, E.; Palmer, T.M.; Yarwood, S.J., *Trends Pharmacol. Sci*., **36**, 203 - 214 (2015): "The Future of EPAC-targeted Therapies: Agonism versus Antagonism"

Rehmann, H., *Sci. Rep.*, 3:3032 (2013): "Epac-Inhibitors: Facts and Artefacts"

Chen, H.; Tsalkova, T.; Mei, F.C.; Hu, Y.; Cheng, X.; Zhou, J., *Bioorg. Med. Chem. Lett.*, **22**, 4038 - 4043 (2012): "5-Cyano-6-oxo-1,6-dihydro-pyrimidines as Potent Antagonists Targeting Exchange Proteins Directly Activated by cAMP"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