
Product Data Sheet

Product Name: Ro 31-8220

Cat. No.: GC17322

Chemical Properties

Cas. No. 125314-64-9

Chemical Name 3-[3-[4-(1-methylindol-3-yl)-2,5-dioxopyrrol-3-yl]indol-1-yl]propyl carbamimidothioate

SMILES CN1C=C(C2=CC=CC=C21)C3=C(C(=O)NC3=O)C4=CN(C5=CC=CC=C54)CCCSC(=N)NFormula $C_{25}H_{23}N_5O_2S$ M.Wt 457.55Solubility Soluble in DMSO Storage Store at $-20^{\circ}C$ General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure **Protocol****Cell experiment:**

A neurotoxic concentration of paraoxon ($200\ \mu M$) is added to the granule cell cultures for the indicated time on day in vitro (DIV) 8. The following drugs are added to the granule cell cultures prior to or after paraoxon exposure on DIV 8: Ro-81-3220 ($1\ \mu M$) is added 15 min prior to or 3 h after the addition of paraoxon. TPA ($0.1\ \mu M$) is added 15 min prior to the addition of paraoxon[1].

Animal experiment:

Mice[4]The affects of long-term Ro 31-8220 administration over 4 to 6 weeks in MLP-/- heart failure mice are investigated. All mice are assessed for ventricular performance by echocardiography at the beginning of the study and 6 weeks later. Ro 31-8220 (or vehicle) is injected subcutaneously once per day at a dosage of $6\ mg/kg/d$ [4].

Caution: Product has not been fully validated for medical applications. For research use only.

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References:

- [1]. Wilkinson SE, et al. Isoenzyme specificity of bisindolylmaleimides, selective inhibitors of protein kinase C. *Biochem J.* 1993 Sep 1;294 (Pt 2):335-7.
- [2]. Davies SP, et al. Specificity and mechanism of action of some commonly used protein kinase inhibitors. *Biochem J.* 2000 Oct 1;351(Pt 1):95-105.
- [3]. Tian F, et al. Inhibition of protein kinase C protects against paraoxon-mediated neuronal cell death. *Neurotoxicology.* 2007 Jul;28(4):843-9. Epub 2007 Apr 20.
- [4]. Hambleton M, et al. Pharmacological- and gene therapy-based inhibition of protein kinase Calpha/beta enhances cardiac contractility and attenuates heart failure. *Circulation.* 2006 Aug 8;114(6):574-82.

Background

Ro 31-8220 is a selective inhibitor of protein kinase C (PKC) with IC₅₀ values of 5, 24, 14, 27, and 24 nM for PKC α , PKC β I, PKC β II, PKC γ and PKC ϵ , respectively [1].

PKC is a monomeric Ca²⁺- and phospholipid-dependent Ser/Thr protein kinases and plays an important role in growth factor-activated signaling and malignant transformation.

Ro 31-8220 is a selective inhibitor of PKC. Also, Ro 31-8220 increased growth factor-stimulated expression of c-Jun but inhibited MKP-1 and c-Fos expression. Ro-31-8220 strongly stimulated the

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stress-activated protein kinase JNK1 in a PKC-independent way [2]. In peripheral blood mononuclear cells, Ro 31-8220 inhibited the production of mitogen-induced interleukin (IL) -2 and IL-2-dependent T lymphoblast proliferation with IC50 values of 80 and 350 nM, respectively. Also, Ro 31-8220 (400 nM) inhibited IL-2R α (CD25) expression by 27%, which suggested that Ro 31-8220 inhibited early and late T cell activation [3].

In rat adipocytes and L6 myotubes, RO 31-8220 activated c-Jun N-terminal kinase (JNK) and glycogen synthase (GS) and stimulated glucose incorporation into glycogen. While, RO 31-8220 inhibited the activity of extracellular response kinases 1 and 2 (ERK1/2) in a PKC-independent way [4].

References:

- [1]. Wilkinson SE, Parker PJ, Nixon JS. Isoenzyme specificity of bisindolylmaleimides, selective inhibitors of protein kinase C. *Biochem J*, 1993, 294 (Pt 2): 335-337.
- [2]. Beltman J, McCormick F, Cook SJ. The selective protein kinase C inhibitor, Ro-31-8220, inhibits mitogen-activated protein kinase phosphatase-1 (MKP-1) expression, induces c-Jun expression, and activates Jun N-terminal kinase. *J Biol Chem*, 1996, 271(43): 27018-27024.
- [3]. Geiselhart L, Conti DJ, Freed BM. RO 31-8220, a novel protein kinase C inhibitor, inhibits early and late T cell activation events. *Transplantation*, 1996, 61(11): 1637-1642.
- [4]. Standaert ML, Bandyopadhyay G, Antwi EK, et al. RO 31-8220 activates c-Jun N-terminal kinase and glycogen synthase in rat adipocytes and L6 myotubes. Comparison to actions of insulin.

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