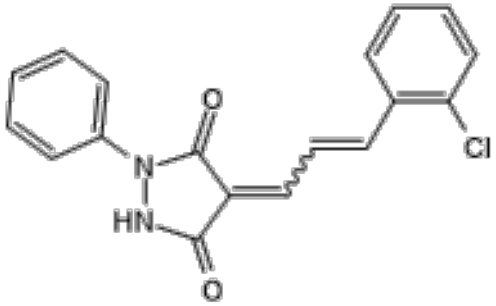
Product Data Sheet

Product Name: CPYPP
Cat. No.: GC50065

Chemical Properties

Cas. No.	310460-39-0		
SMILES	O=C(N(C3=CC=CC=C3)NC2=O)/C2=C\C=C\C1=C(Cl)C=CC=C1		
Formula	$C_{18}H_{13}ClN_2O_2$	M.Wt	324.76
Solubility	DMSO: 50 mM	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°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 [1]:

Cell lines	Spleen cells of BALB/c mice
Preparation Method	Spleen cells of BALB/c mice (1 × 107/ml) were incubated in RPMI1640 medium supplemented with 0.5% BSA or 10% FCS in the presence or absence of 100 μM CPYPP. 1 or 5 hr of incubation at 37°C.

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Reaction Conditions	100μM for 1 hour or 5 hours
Applications	CPYPP was nontoxic when applied to spleen cells at 100 μM .

Animal experiment [2]:

Animal models	male C57BL/6J mice
Preparation Method	Mice were randomized into four groups (n = 6): the saline + vehicle group, LPS + vehicle group, saline + CPYPP group, and LPS + CPYPP group. ALI was induced by intraperitoneal (i.p.) injection of LPS (10 mg/kg) body weight; The mice in the LPS + vehicle and LPS + CPYPP groups received CPYPP (250 mg/kg) or an equivalent volume of vehicle via i.p. injection 10 min after LPS administration. The mice in the saline + vehicle and saline + CPYPP groups received CPYPP (250 mg/kg) or an equivalent volume of vehicle via i.p. injection 10 min after saline administration.
Dosage form	Intraperitoneal injection, 250 mg/kg
Applications	CPYPP-treated mice had decreased lung injury scores compared with vehicle-treated mice. Furthermore, CPYPP-treated mice exhibited significantly decreased MPO activity and W/D ratios, which indicated decreased pulmonary edema.

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References:

[1]: Nishikimi?A, Uruno?T, Duan?X, Cao?Q, Okamura?Y, Saitoh?T, et al.?Blockade of inflammatory responses by a small-molecule inhibitor of the Rac activator DOCK2. Chem Biol?2012;19:488-97.
[2]: Xu, X., Su, Y., Wu, K., Pan, F. & Wang, A. DOCK2 contributes to endotoxemia-induced acute lung injury in mice by activating proinflammatory macrophages. Biochem. Pharmacol. 181, 114399 (2021).

Background

CPYPP bound to DOCK2 DHR-2 domain (DOCK2 $^{DHR-2}$) in a reversible manner and inhibited its catalytic activity[1].

CPYPP inhibited the guanine nucleotide exchange factor (GEF) activity of DOCK2DHR-2 for Rac1 in a dose-dependent manner, with a half-maximal inhibitory concentration (IC_{50}) of 22.8 ± 2.4 μM. This inhibitory activity was independent on length of preincubation time, ranging from 2 min to 30 min. In addition, CPYPP was nontoxic when applied to spleen cells or thymoma cells (BW5147α-β-) at 100 μM for 3 hr or 3 days, respectively [1]. Pre-treatment of human neutrophils with CPYPP, a small molecule inhibitor of the DHR-2 domain of DOCK proteins and thus of the Rac GEF activity of human DOCK2 and DOCK5, significantly impaired neutrophil chemotaxis and ROS production [2].

CPYPP effectively decreased the secretion and gene expression of TNF-α, IL-1β and IL-6 in the lungs, suggested effects of DOCK2 on endotoxemia-induced inflammatory responses in mice. CPYPP remarkably inhibited the infiltration of total cells, macrophages and neutrophils into the bronchoalveolar lavage fluid [3]. A reseach found out that a joint usage of both CPYPP and C25-140 revealed a better consequence compared to monotherapy against hepatic I/R injury [4].

References:
[1]. Nishikimi?A, Uruno?T, Duan?X, Cao?Q, Okamura?Y, Saitoh?T, et al.?Blockade of inflammatory responses by a small-molecule inhibitor of the Rac activator DOCK2. Chem Biol?2012;19:488-97.
[2]. Moens, L., Gouwy, M., Bosch, B. et al. 2019. Human DOCK2 deficiency: report of a novel mutation and evidence for neutrophil dysfunction. J. Clin. Immunol. 39:298.
[3]. Xu, X., Su, Y., Wu, K., Pan, F. & Wang, A. DOCK2 contributes to endotoxemia-induced acute

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lung injury in mice by activating proinflammatory macrophages. Biochem. Pharmacol. 181, 114399 (2021).
[4]. Zuotian Huang, Junliang Pua, Yunhai Luo, et al. FAM49B, restrained by miR-22, relieved hepatic ischemia/reperfusion injury by inhibiting TRAF6/IKK signaling pathway in a Rac1-dependent manner. Molecular Immunology.143, 2022, 135-146.

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