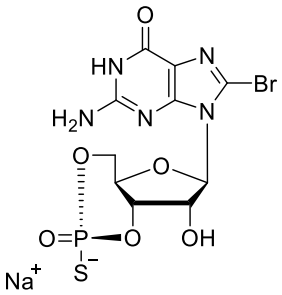
BIOLOG - LIFE SCIENCE INSTITUTE -

Technical Information about Rp-8-Br-cGMPS

Membrane-permeant and metabolically stable inhibitor for cGMP-dependent protein kinases

Update: July 06, 2018 HJ



Abbreviation: **Rp-8-Br-cGMPS**

Formula	CAS No.	Molecular Weight	UV	BIOLOG Cat.No.
$C_{10}H_{10}BrN_5O_6PS{\cdot}Na$	[150418-07-8]	462.2	λ_{max} 260 nm / ε 16200 / pH 7	B 005

Name: 8- Bromoguanosine- 3', 5'- cyclic monophosphorothioate, Rp- isomer

Description: Rp-8-Br-cGMPS is an analogue of the parent compound cyclic GMP in which the hydrogen in position 8 of the nucleobase is replaced by bromine and the equatorial one of the two exocyclic oxygen atoms in the cyclic phosphate moiety is modified by sulfur. The suffix "p" indicates that R/S nomenclature refers to phosphorus.

Properties: Rp-8-Br-cGMPS is a combination of the PDE-resistant protein kinase G inhibitor Rp-cGMPS with the widely used 8-bromo cyclic GMP resulting in a membrane-permeant cyclic GMP antagonist which is not metabolized by mammalian cyclic nucleotide phosphodiesterases.
Rp-8-Br-cGMPS is about 1.5 times more lipophilic compared to 8-Br-cGMP, and 2.5 times and 3.5 times more compared to Rp-cGMPS and cGMP, respectively.

Application: Experience shows that applicable concentrations of Rp-8-Br-cGMPS depend on the type of biosystem, its membrane properties and kinase content. A main application for Rp-8-Br-cGMPS is to eliminate the first messenger-stimulated phosphorylation by cyclic GMP-dependent protein kinase. For this purpose preincubation (e.g. 20 min) is important, since the production of intracellular cyclic GMP initiated by a first messenger is much faster than the antagonist can penetrate the membrane when given extracellularly. Since Rp-8-Br-cGMPS is hydrolytically stable in mammalian and many other systems there is no danger of degradation during incubation periods.

Specification: Lyophilized or crystallized sodium salt. The free acid or other salt forms are available upon request. Equal concentrations of Rp-8-Br-cGMPS can appear very different in volume due to sensitivity of the lyophilized form to humidity and the compound can even contract to small volume droplets. Normally the product is located in the conical bottom of the tube. Micromolar quantities are determined by UV at λ_{max}. The agonistic Sp-isomer is offered as well (Sp-8-Br-cGMPS, Cat. No. B 006).

Purity: Typical analysis is better than 99% (HPLC / UV / 260 nm). The product is not sterile and has not been tested for endotoxins.
Caution: Since even minor impurities of 8-Br-cGMP (0.2%) or Sp-8-Br-cGMPS can already activate protein kinase and compete with the antagonistic effect of the Rp-isomer it is very important to work with strictly pure compounds concerning cyclic nucleotide contaminants. Therefore, Rp-8-Br-cGMPS is specially checked for absence of both, Sp-8-Br-cGMPS and 8-Br-cGMP (< 0.05% when packed). However, we cannot guarantee total absence of 8-Br-cGMP due to its formation during prolonged storage.

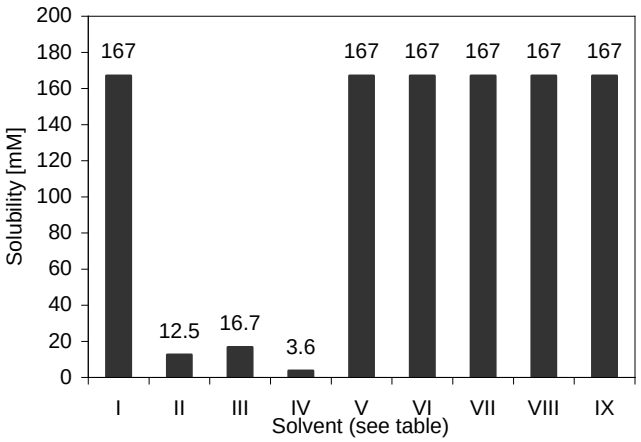
Stability and Storage: Rp-8-Br-cGMPS has sufficient stability at room temperature and does not need special care during handling or shipment. Nevertheless, we recommend that the compound should be stored in the freezer, for longer storage periods preferably in freeze-dried form, since desulfurization yielding 8-Br-cGMP can occur slowly. This normally rather slow sulfur/oxygen exchange is accelerated by oxidizing agents.

Toxicity and Safety: Since cyclic GMP has multiple tasks in every organism it is very likely that lipophilic cGMP analogues will interfere with many cell regulation processes *in vivo*. However, due to the rather small quantities to work with no health hazards have been reported. Nevertheless please keep in mind that the *in vivo* properties of these compounds 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!

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de

Solubility: Detailed information on the solubility of Rp-8-Br-cGMPS in water and various buffers are listed in the solubility chart below. Concentrations have been determined at ambient temperature and can be considered as minimum concentrations usually obtainable, however, slight batch-to-batch variations cannot be ruled out. When opening the tube please make sure that no substance is lost within the cap. Please rinse tube walls carefully and preferably use ultrasonic or vortex to achieve total and uniform mixing.

No.	Solvent	Solubility [mM]
I	H_2O	167
II	DMSO	12.5
III	DMF	16.7
IV	Ethanol 96%	3.6
V	Methanol	167
VI	PBS, pH 7.4	167
VII	100 mM Na_2HPO_4, pH 7.0	167
VIII	25 mM Hepes/NaOH, pH 7.2	167
IX	25 mMTris/HCl, pH 7.4	167



Selected References for Rp-8-Br-cGMPS:
For a detailed list please inquire or visit our website (http://www.biolog.de).

Paquet-Durand, F.; Hauck, S.M.; van Veen, T.; Ueffing, M.; Ekström, P., *J. Neurochem.*, **108**, 796 - 810 (2009): "PKG Activity Causes Photoreceptor Cell Death in Two Retinitis pigmentosa Models"

Brown, R.L.; Strassmeier, T.; Brady, J.D.; Karpen, J.W., *Curr. Pharmaceut. Design*, **12**, 3597 - 3613 (2006): "The Pharmacology of Cyclic Nucleotide-gated Channels: Emerging from the Darkness"

Gragasin, F.S.; Michelakis, E.D.; Hogan, A.; Moudgil, R.; Hashimoto, K.; Wu, X.C.; Bonnent, S.; Haromy, A.; Archer, S.L., *FASEB Journal*, **18**, 1382 - 1391 (2004): " The Neurovascular Mechanism of Clitoral Erection: Nitric Oxide and cGMP-stimulated Activation of BKCa Channels"

Huang, C.C.; Chan, S.H.H.; Hsu, K.S., *Mol. Pharmacol.*, **64**, 521 - 532 (2003): "cGMP/Protein Kinase G-dependent Potentation of Glutamatergic Transmission Induced by Nitric Oxide in Immature Rat Rostral Ventrolateral Medulla Neurons in Vitro"

Schmidtko, A.; Ruth, P.; Geisslinger, G.; Tegeder, I., *Nitric Oxide-Biol. Chem.*, **8**, 89 - 94 (2003): "Inhibition of Cyclic Guanosine 5'-Monophosphate-dependent Protein Kinase I (PKG-I) in Lumbar Spinal Cord Reduces Formalin-induced Hyperalgesia and PKG Upregulation"

Alencar, J.L.; Lobysheva, I.; Geffard, M.; Sarr, M.; Schott, C.; Schini-Kerth, V.B.; Nepveu, F.; Stoclet, J.C.; Muller, B., *Mol. Pharmacol.*, **63**, 1148 - 1158 (2003): "Role of S-nitrosation of Cysteine Residues in Long-lasting Inhibitory Effect of Nitric Oxide on Arterial Tone"

Carvajal, J.A.; Thompson, L.P.; Weiner, C.P., *Am. J. Obstet. Gynecol.*, **188**, 84 - 91 (2003): "Chorion-induced Myometrial Relaxation is Mediated by Large-Conductance Ca^{2+}-activated K^+ Channel Opening in the Guinea Pig"

Sellak, H.; Yang, X.; Cao, X.; Cornwell, T.; Soff, G.A.; Lincoln, T., *Circ. Res*., **90**, 405 - 412 (2002): "Sp1 Trancription Factor as a Molecular Target for Nitric Oxide- and Cyclic Nucleotide-Mediated Suppression of cGMP-dependent Protein Kinase-1 α Expression in Vascular Smooth Muscle Cells"

Monfort, P.; Munoz, M.D.; Kosenko, E.; Felipo, V., *J. Neurosci.*, **22**, 10116 - 10122 (2002): "Long-Term Potentiation in Hippocampus Involves Sequential Activation of Soluble Guanylate Cyclase, cGMP-dependent Protein Kinase, and cGMP-degrading Phosphodiesterase"

Song, R.P.; Mahidhara, R.S.; Liu, F.; Ning, W.; Otterbein, L.E.; Choi, A.M. K., *Am. J. Respir. Cell Mol. Biol.*, **27**, 603 - 610 (2002): "Carbon Monoxide Inhibits Human Airway Smooth Muscle Cell Proliferation via Mitogen-activated Protein Kinase Pathway"

Tegeder, I.; Schmidtko, A.; Niederberger, E.; Ruth, P.; Geisslinger, G., *Neurosci. Lett.*, **332**, 146 - 150 (2002): "Dual Effects of Spinally Delivered 8-Bromo-cyclic Guanosine Monophosphate (8-Bromo-cGMP) in Formalin-induced Nociception in Rats"

Cook, A.L.M.; Frydenberg, M.; Haynes, J.M., *Cell. Signal.*, **14**, 1023 - 1029 (2002): "Protein Kinase G Activation of K-ATP Channels in Human-cultured Prostatic Stromal Cells"

Andersson, J.A.; Uddman, R.; Cardell, L.O., *Allergy*, **57**, 1008 - 1012 (2002): "Hemin, a Heme Oxygenase Substrate Analog, Both Inhibits and Enhances Neutrophil Random Migration and Chemotaxis"

Layland, J.; Li, J.M.; Shah, A.M., *J. Physiol.-London*, **540**, 457 - 467 (2002): "Role of Cyclic GMP-dependent Protein Kinase in the Contractile Response to Exogenous Nitric Oxide in Rat Cardiac Myocytes"

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de

Centonze, D.; Pisani, A.; Bonsi, P.; Giacomini, P.; Bernardi, G.; Calabresi, P., *J. Neurosci.*, **21**, 1393 - 1400 (2001): "Stimulation of Nitric Oxide-cGMP Pathway Excites Striatal Cholinergic Interneurons via Protein Kinase G Activation"

Carvajal, J.A.; Aguan, K.; Thompson, L.P.; Buhimschi, I.A.; Weiner, C.P., *J. Pharmacol. Exp. Ther.*, **297**, 181 - 188 (2001): "Natriuretic Peptide-induced Relaxation of Myometrium from the Pregnant Guinea Pig is not Mediated by Guanylate Cyclase Activation"

Takeuchi, T.; Sugimoto, K.; Morimoto, H.; Fujita, A.; Hata, F., *Jpn. J. Pharmacol.*, **86**, 390 - 398 (2001): "Mechanism of a Nitric Oxide Donor NOR 1-induced Relaxation in Longitudinal Muscle of Rat Proximal Colon"

Homer, K. L.; Wanstall, J. C., Br. *J. Pharmacol.*, 131, 673 - 682 (2000): "Cyclic GMP-independent Relaxation of Rat Pulmonary Artery by Spermine NONOate, a Diazeniumdiolate Nitric Oxide Donor"

Elferink, J.G.R.; de Koster, B. M., *Immunopharmacology*, **38**, 229 - 236 (1998): "*N*-Acetylcysteine Causes a Transient Stimulation of Neutrophil Migration"

Cousson, A.; Vavasseur, A.; *Planta*, **206**, 308 - 314 (1998): "Putative Involvement of Cytosolic Ca^{2+} and GTP-Binding Proteins in Cyclic-GMP-mediated Induction of Stomatal Opening by Auxin in Commelina Communis L"

Wei, J.Y.; Cohen, E.D.; Genieser, H.-G.; Barnstable, C.J.; *J. Mol. Neurosci*., **10**, 53 - 64 (1998): "Substituted cGMP Analogs Can Act as Selective Agonists of the Rod Photoreceptor cGMP-Gated Cation Channel"

Nakazawa, M.; Watanabe, Y.; Toyosato, A.; Yoshida, Y.; Higuchi, H.*; Naunyn-Schmiedebergs Arch. Pharmacol.*, **358**, Suppl. 2, XIIIth. Int. Congr. Pharmacol. Munich 1998, R 662, P 22.14: "Effects of Calcium Concentration on Rp-8-Br-cGMPS-induced Inhibition of Relaxation by Nitroprusside in the Rat Aorta"

Wegener, J.W.; Gath, I.; Förstermann, U.; Nawrath, H.; *Br. J. Pharmacol*., **122**, 1523 - 1529 (1997): "Activation of Soluble Guanylyl Cyclase by YC-1 in Aortic Smooth Muscle But Not In Ventricular Myocardium From Rat"

Elferink, J.G.R.; Daha, M.R.; de Koster, B.M.; *CMLS Cell. Mol. Life Sci.*, **53**, 593 - 599 (1997): "A Cyclic GMP- and G-Kinase-dependent Effect of Azathioprine on Migration by Human Neutrophils"

Forloni, G.; Lucca, E.; Angeretti, N.; Chiesa, R.; Vezzani, A.; *J. Neurochem*. **68**, 319 - 327 (1997): "Neuroprotective Effect of Somatostatin on Nonapoptotic NMDA-Induced Neuronal Death- Role of Cyclic GMP"

Nakamura, A.; Fujita, M.; Shiomi, H.; *Brit. J. Pharmacol*., **117**, 407 - 412 (1996): "Involvement of Endogenous Nitric Oxide in the Mechanism of Bradykinin-induced Peripheral Hyperalgesia"

Murphy-Ullrich, J. E.; Pallero, M.A.; Boerth, N.; Greenwood, J.A.; Lincoln, T.M.; Cornwell, T.L.; *J. Cell Sci*., **109**, 2499 - 2508 (1996): "Cyclic GMP-dependent Protein Kinase is Required for Thrombospondin and Tenascin Mediated Focal Adhesion Disassembly"

Bito, H.; Deisseroth, K.; Tsien, R.W.; *Cell* **87**, 1203 - 1214 (1996): "CREB Phosphorylation and Dephosphorylation: A Ca^{2+}- and Stimulus Duration-Dependent Switch for Hippocampal Gene Expression"

Armstead, W.M.; *Am. J. Physiol*., **40**, H166 - H172 (1996): "cGMP and cAMP in Prostaglandin-induced Pial Artery Dilation and Increased CSF Opioid Concentration"

Rooney, T.A.; Joseph, S.K.; Queen, C.; Thomas, A.P.; *J. Biol. Chem*., **271**, 19817 - 19825 (1996): "Cyclic GMP Induces Oscillatory Calcium Signals in Rat Hepatocytes"

Blitzer, R.D.; Wong, T.; Nouranifar, R.; Iyengar, R.; Landau, E.M.; *Neuron*, **15**, 1403 - 1414 (1995): "Postsynaptic cAMP Pathway Gates Early LTP in Hippocampal CA1 Region"

Barger, S.W.; Fiscus, R.R.; Ruth, P.; Hofmann, F.; Mattson, M.P.; *J. Neurochem*., **64**, 2087 - 2096 (1995): "Role of Cyclic GMP in the Regulation of Neuronal Calcium and Survival by Secreted Forms of ß-Amyloid Precursor"

Bäumner, D.; Nawrath, H.; *Eur. J. Pharmacol*., **273**, 295 - 298 (1995): "Effects of Inhibitors of cGMP-dependent Protein Kinase in Atrial Heart and Aortic Smooth Muscle From Rats"

Brown, J.F.; Hanson, P.J.; Whittle, B.J.R.; *Biochem. Biophys. Res. Commun.*, **195**, 1354 - 1359 (1995): "The Nitric Oxide Donor, S-Nitroso-N-acetyl-penicillamine, Inhibits Secretory Activity in Rat Isolated Parietal Cells"

Bowler,C.; Neuhaus, G.; Yamagata, H.; Chua, N.- H., *Cell*, **77**, 73 - 81 (1994): "Cyclic GMP and Calcium Mediate Phytochrome Phototransduction"

Ohigashi, T.; Brookins, J.; Fisher, J.W., *J. Clin. Invest*., **92**, 1587 - 1591 (1994): "Interaction of Nitric Oxide and Cyclic Guanosine 3',5'- Monophosphate in Erythropoietin Production"

Cornwell, T.L.; Arnold, E.; Boerth, N.J.; Lincoln, T.M., *Am. J. Physiol*., **267**, C1405 - C1413 (1994): "Inhibition of Smooth Muscle Cell Growth by Nitric Oxide and Activation of cAMP-dependent Protein Kinase by cGMP"

Zhuo, M.; Hu,Y.; Schultz, C.; Kandel, E.R.; Hawkins, R.D., *Nature* **368**, 635 - 639 (1994): "Role of Guanylyl Cyclase and cAMP-dependent Protein Kinase in Long-term Potentiation"

Ouedrago, S.; Tschöpl, M.; Stoclet, J.-C.; Bucher, B., *Br. J. Pharmacol*., **112**, 867 - 872 (1994): "Effects of cyclic GMP and Analogues on Neurogenic Transmission in the Rat Tail Artery"

Nakazawa, M.; Imai, S., *Eur. J. Pharmacol*., **253**, 179 - 181 (1994): "Rp-8-Br-Guanosine- 3', 5' - cyclic Monophosphorothioate Inhibits Relaxation Elicited by Nitroglycerin in Rabbit Aorta"

Chao, A.C.; de Sauvage, F.J.; Dong, Y.-J.; Wagner, J.A.; Goeddel, D.V.; Gardner, P., *EMBO J*., **13**, 1065 - 1072 (1994): "Activation of Intestinal CFTR Cl^- Channel by Heat-stable Enterotoxin and Guanylin Via cAMP-dependent Protein Kinase"

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de

Butt, E.; Van Bemmelen, M.; Fischer, L.; Walter, U.; Jastorff, B., *FEBS Lett*., **263**, 47-50 (1990): "Inhibition of cGMP-dependent Protein Kinase by Rp-Guanosine 3',5'-monophosphorothioates"

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de