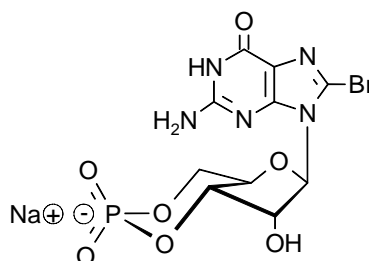


Technical Information about 8-Bromo-cGMP

Potent activator of cGMP-dependent protein kinases and cGMP-gated ion channels

Update: August 30, 2011 HJ



Abbreviation: 8-Br-cGMP

Formula	CAS No.	Molecular Weight	UV	BIOLOG Cat. No.
C ₁₀ H ₁₆ BrN ₅ O ₇ P·Na	[51116-01-9]	446.1	λ _{max} 260 nm / ε 16200 / pH 7	B 004 / B 004 E

Name: 8- Bromoguanosine- 3', 5'- cyclic monophosphate, cyclic 8- bromoguanosine- 3', 5'- monophosphate, 8- bromoguanosine- 3', 5'- monophosphate

Description: 8-Br-cGMP is an analogue of the natural signal molecule cyclic GMP in which the hydrogen in position 8 of the heterocyclic nucleobase is replaced by bromine.

Bulk Supply: 8-Br-cGMP can be offered in multigram quantities at extremely competitive prices. Please ask for a corresponding quotation.

Properties: 8-Br-cGMP is an activator of cGMP-dependent protein kinase type I α with preferential binding to its slow exchanging site, showing increased activation potential compared to the parent compound cGMP. The K_a for the corresponding isozyme I β is approximately 10 times higher.

The compound is a bad activator of both, type I and II of cAMP-dependent protein kinase with more than two magnitudes of order difference to cGMP kinase.

8-Br-cGMP is also a potent cGMP agonist for cGMP-dependent ion channels, with 10 times higher potency compared to cGMP.

Its increased lipophilicity allows for membrane permeability in several biosystems. If permeability is not sufficient for your application, please use the highly lipophilic 8-pCPT-cGMP (Cat. No.: C 009), PET-cGMP (Cat. No.: P 001) or 8-Br-PET-cGMP (Cat. No.: P 003).

In comparison to cyclic GMP 8-Br-cGMP is degraded by cyclic nucleotide-dependent phosphodiesterases much more slowly, however, in contrast to general opinion it is not completely stable. So it is possible that disturbing metabolites can appear, especially during long term incubation experiments. In these cases we recommend again 8-pCPT-cGMP.

Specification: Lyophilized or crystallized sodium salt. The free acid or other salt forms are available upon request. Equal concentrations of 8-Br-cGMP can appear very different in volume due to sensitivity of the lyophilized form to humidity. 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}.

Purity: Typical analysis is better than 98% (Economy Grade) and 99% (Fluorescence Grade) respectively (HPLC / UV / 260 nm). Traces of fluorescent impurities inevitably formed during production have been removed by an additional purification step for the Fluorescence Grade. The product is not sterile and has not been tested for endotoxins.

Stability and Storage: 8-Br-cGMP does not need special care during handling and shipment. Nevertheless, we recommend that the compound should be stored in the freezer, for longer storage periods preferably in freeze-dried form.

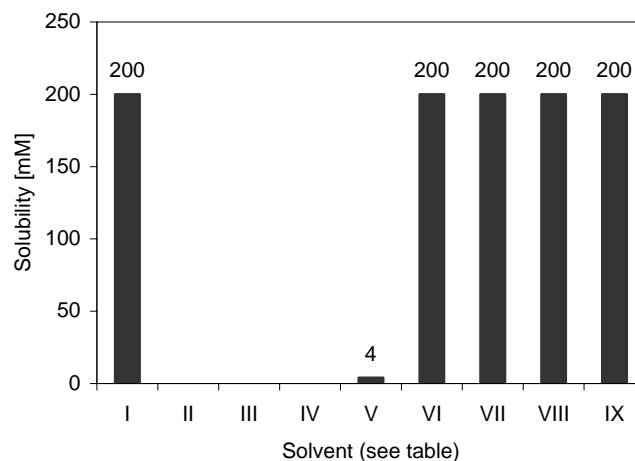
Toxicity and Safety: Since cyclic GMP has multiple tasks in every organism it is possible that cGMP analogues will interfere with many cell regulation processes *in vivo*. However, due to the rather small quantities to work with no health hazards have been reported. Nevertheless please keep in mind that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

Solubility: Detailed information on the solubility of 8-Br-cGMP 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 ₂ O	200
II	DMSO	0
III	DMF	0
IV	Ethanol 96%	0
V	Methanol	4
VI	PBS, pH 7.4	200
VII	100 mM Na ₂ HPO ₄ , pH 7.0	200
VIII	25 mM HEPES/NaOH, pH 7.2	200
IX	25 mM Tris/HCl, pH 7.4	200



Selected References for 8-Br-cGMP: Since 8-Br-cGMP is a well known biochemical tool there exist numerous citations for almost every biosystem and it is impossible to list them all. Therefore, the following papers give basic information about different aspects of 8-Br-cGMP:

Protein Kinases:

Corbin, J.D.; Øgreid, D.; Miller, J.P.; Suva, R.H.; Jastorff, B.; Døskeland, S.O., *J. Biol. Chem.*, **261**, 1208 - 1214 (1986): "Studies of cGMP Analog Specificity and Function of the Two Intrasubunit Binding Sites of cGMP-dependent Protein Kinase"

Wolfe, L.; Corbin, J.D.; Francis, S.H., *J. Biol. Chem.*, **264**, 7734 - 7741 (1989): "Characterization of a Novel Isozyme of cGMP-dependent Protein Kinase from Bovine Aorta"

Sekhar, K.R.; Hatchett, R.J.; Shabb, J.B.; Wolfe, L.; Francis, S.H.; Wells, J.W.; Jastorff, B.; Butt, E.; Chakinala, M.M.; Corbin, J.D., *Mol. Pharmacol.*, **42**, 103 - 108 (1992): "Relaxation of Pig Coronary Arteries By New and Potent cGMP Analogs That Selectively Activate Type I α Compared to Type I β cGMP-Dependent Protein Kinase"

Vaandrager, A.B.; Bot, A.G.M.; De Jonge, H.R., *Gastroenterology*, **112**, 437 - 443 (1997): "Guanosine 3',5'-Cyclic Monophosphate-Dependent Protein Kinase II Mediates Heat-Stable Enterotoxin-Provoked Chloride Secretion in Rat Intestine"

Taylor, M.K.; Ahmed, R.; Begley, M.; Uhler, M.D., *J. Biol. Chem.*, **277**, 37242 - 37253 (2001): "Autoinhibition and Isoform-specific Dominant Negative Inhibition of the Type II cGMP-dependent Protein Kinase"

Ion channels:

Zimmerman, A.L.; Yamanaka, G.; Eckstein, F.; Baylor, D.A.; Stryer, L., *Proc. Natl. Acad. Sci. USA*, **82**, 8813 - 8817 (1985): "Interaction of Hydrolysis-resistant Analogs of Cyclic GMP with the Phosphodiesterase and Light - sensitive Channel of Retinal Rod Outer Segments"

Tanaka, J.C.; Eccleston, J.F.; Furman, R.E., *Biochemistry* **28**, 2776 - 2784 (1989): "Photoreceptor Channel Activation by Nucleotide Derivatives"

Scott, S.-P.; Tanaka, J. C., *Biochemistry*, **34**, 2338 - 2347 (1995): "Molecular Interactions of 3',5'-Cyclic Purine Analogues with the Binding Site of Retinal Rod Ion Channels"

Wei, J.-Y.; Cohen, E.D.; Yan, Y.-Y.; Genieser, H.-G.; Barnstable, C.J., *Biochemistry* **35**, 16815 - 16823 (1996): "Identification of Competitive Antagonists of the Rod Photoreceptor cGMP-Gated Cation Channel: β -Phenyl-1, N(2)-Etheno-Substituted cGMP Analogues as Probes of the cGMP-Binding Site"

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"

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"

Phosphodiesterases:

Erneux, C.; Miot, F.; Van Haastert, P.J.M.; Jastorff, B., *J. Cyclic Nucleotide Protein Phosphorylation Res.*, **10**, 463 - 472 (1985): "The Binding of Cyclic Nucleotide Analogs to a Purified Cyclic GMP- Stimulated Phosphodiesterase from Bovine Adrenal Tissue"

Braumann, T.; Erneux, C.; Petridis, G.; Stohrer, W.D.; Jastorff, B., *Biochim. Biophys. Acta*, **871**, 199 - 206 (1986): "Hydrolysis of Cyclic Nucleotides by a Purified cGMP-stimulated Phosphodiesterase: Structural Requirements for Hydrolysis"

Erneux, C.; Miot, F., *Methods Enzymol.*, **159**, 520 - 530 (1988): "Cyclic Nucleotide Analogs Used to Study Phosphodiesterase Catalytic and Allosteric Sites"

Hebert, M.C.; Schwede, F.; Jastorff, B.; Cote, R. H., *J. Biol. Chem.*, **273**, 5557 - 5565 (1998): "Structural Features of the Noncatalytic cGMP Binding Sites of Frog Photoreceptor Phosphodiesterase Using cGMP Analogs"

Jäger, R.; Schwede, F.; Genieser, H.-G.; Koesling, D.; Russwurm, M., *Br. J. Pharmacol.*, **161**, 1645 - 1660 (2010): "Activation of PDE2 and PDE5 by Specific GAF Ligands: Delayed Activation of PDE5"

Lipophilicity & Membrane Permeability:

For a comparison of the lipophilicity of different cyclic nucleotides, please refer to our corresponding website: http://www.biolog.de/technical_info/Lipophilicity_Data/.

General Aspects and Applications:

Maeda, T.; Murase, N.; Subbotin, V.; Sakamoto, T.; Yamada, T.; Terakura, M.; Todo, S., *Transplantation*, **66**, 844 - 851 (1998): "Analogues of Cyclic Nucleotides in Rat Liver Preservation"

Hillinger, S.; Schmid, R. A.; Sandera, P.; Stammberger, U.; Schreiner, D.; Schoedon, G.; Weder, W., *Ann. Thorac. Surg.*, **68**, 1138 - 1143 (1999): "8-Br-cGMP is Superior to Prostaglandin E1 for Lung Preservation"

Schwede, F.; Maronde, E.; Genieser, H.-G.; Jastorff, B., *Pharmacol. Ther.*, **87**, 199 - 226 (2000): "Cyclic Nucleotide Analogs as Biochemical Tools and Prospective Drugs"

Sawa, T.; Zaki, M.H.; Okamoto, T.; Akuta, T.; Tokutomi, Y.; Kim-Mitsuyama, S.; Ihara, H.; Kobayashi, A.; Yamamoto, M.; Fujii, S.; Arimoto, H.; Akaike, T., *Nature Chem. Biol.*, **3**, 727 - 735 (2007): "Protein S-guanylation by the Biological Signal 8-nitroguanosine 3',5'-cyclic Monophosphate"

Voisin, P.; Bernard, M., *J. Neurochem.*, **110**, 318 - 327 (2009): "Cyclic AMP-dependent Activation of Rhodopsin Gene Transcription in Cultured Retinal Precursor Cells of Chicken Embryo"

Kurauchi, Y.; Hisatsune, A.; Isohama, Y.; Sawa, T.; Akaike, T.; Shudo, K.; Katsuki, H., *J. Neurochem.*, **116**, 323 - 333 (2011): "Midbrain Dopaminergic Neurons Utilize Nitric Oxide/cyclic GMP Signaling to Recruit ERK that Links Retinoic Acid Receptor Stimulation to Up-regulation of BDNF"