- LIFE SCIENCE INSTITUTE -

BIOLOG

Epac-related Research Tools

Second Messenger and Signal Transduction Research
High Purity Nucleotide & Nucleoside Analogues

- *Unique Collection of Cyclic Nucleotides*
- *Inhibitors and Activators of Protein Kinases A and G*
- *Specific Epac Modulators*
- *Widest Selection of NAD^+ and cADPR Analogues*
- *c-diGMP and c-diAMP, Derivatives and Metabolites*
- *Nucleoside Mono-, Di-, Tri- and Polyphosphates*
- *Fluorescent and Biotinylated Analogues*
- *Affinity Chromatography Gels*
- *Bulk and Custom Syntheses*

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Catalogue Content

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BIOLOG Product List

Epac- relevant Structures

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8- (6- Aminohexylamino)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-AHA-2'-O-Me-cAMP)	A 099	5
8- Bromo- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-Br-2'-O-Me-cAMP)	B 022	5
8- Bromo- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate, acetoxymethyl ester (8-Br-2'-O-Me-cAMP-AM)	B 028	6
8- Bromo- 2'- O- methyladenosine- 3', 5'- cyclic monophosphorothioate, Sp-isomer (Sp-8-Br-2'-O-Me-cAMPS)	B 031	6
8- (4- Chlorophenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-pCPT-2'-O-Me-cAMP)	C 041	6
8- (4- Chlorophenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate, AM ester (8-pCPT-2'-O-Me-cAMP-AM)	C 051	6
8- (4- CPT)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer (Sp-8-pCPT-2'-O-Me-cAMPS)	C 052	6
8- (2- [DY-547]- aminoethylthio)- 2'- O-methyladenosine- 3', 5'- cyclic monophosphate (8-[DY-547]-AET-2'-O-Me-cAMP)	D 089	6
8- Hydroxy- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-OH-2'-O-Me-cAMP)	H 013	7
8- (4- Hydroxyphenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-pHPT-2'-O-Me-cAMP)	H 010	7
8- (4- Methoxyphenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-pMeOPT-2'-O-Me-cAMP)	M 034	7
2'- O- Methyladenosine- 3', 5'- cyclic monophosphate (2'-O-Me-cAMP)	M 050	7
8- [Pharos-575]- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-[φ-575]-2'-O-Me-cAMP)	P 021	7
Epac 2- selective Agonists		
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PKA- selective agonists that do not activate Epac		
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8- (4- Chlorophenylthio)- 2'- O- methylguanosine- 3', 5'- cyclic monophosphate (8-pCPT-2'-O-Me-cGMP)	C 048	8
2'- O- Methylguanosine- 3', 5'- cyclic monophosphate (2'-O-Me-cGMP)	M 036	8
Selective Epac Inhibitors		
3- [5- (tert.- Butyl)isoxazol- 3- yl]- 2- [2- (3- chlorophenyl)hydrazono]- 3- oxopropanenitrile (ESI-09)	B 133	9
4- Cyclopentyl- 2- (2, 5- dimethylbenzylsulfanyl)- 6- oxo- 1, 6- dihydropyrimidine- 5- carbonitrile (HJC0197)	C 136	9
4- Methylphenyl- 2, 4, 6- trimethylphenylsulfone (ESI-05)	M 092	9
Potential Metabolites of Epac- relevant Structures	Inquire	

Cyclic Nucleotide Affinity Chromatography Gels

	Cat. No.	Page
2'-O-Me-cAMP, immobilized on agarose via ethyl spacer to adenine C-8 (8-AET-2'-O-Me-cAMP-Agarose)	A 195	9
2'-O-Me-cAMP, immobilized on agarose via hexyl spacer to adenine C-8 (8-AHA-2'-O-Me-cAMP-Agarose)	A 057	10
Unmodified control gel		
Ethanolamine, immobilized on agarose (EtOHNH-Agarose)	E 010	10
Additional cyclic nucleotide affinity gels, different ligands, spacers and gel matrices not listed.	Inquire	

Preparation of Stock Solutions

Most BIOLOG products are sold in micromol quantities in order to assist customers with the preparation of stock solutions. In contrast to often troublesome calculations regarding molecular weight, salt form, water content and purity percentages, simply add certain volumes of solvent (mostly water or buffer) and end up already with stock solutions of defined concentrations.
The following table shows how to dissolve the content of a vial with water or buffer in order to obtain defined stock solutions:

Concentration of stock solution	Content of vial					
	1 µmol	**5 µmol**	**10 µmol**	**25 µmol**	**50 µmol**	**100 µmol**
	⇓	⇓	⇓	⇓	⇓	⇓
	Water or buffer volumes to be added to achieve stock concentrations on the left					
	⇓	⇓	⇓	⇓	⇓	⇓
100 mM (1×10^{-1} M)	10 µl	50 µl	100 µl	250 µl	500 µl	1 ml
50 mM (5×10^{-2} M)	20 µl	100 µl	200 µl	500 µl	1 ml	2 ml
20 mM (2×10^{-2} M)	50 µl	250 µl	500 µl	1.25 ml	2.5 ml	5 ml
10 mM (1×10^{-2} M)	100 µl	500 µl	1 ml	2.5 ml	5 ml	10 ml
5 mM (5×10^{-3} M)	200 µl	1 ml	2 ml	5 ml	10 ml	20 ml
1 mM (1×10^{-3} M)	1 ml	5 ml	10 ml	25 ml	50 ml	100 ml
500 µM (5×10^{-4} M)	2 ml	10 ml	20 ml	50 ml	100 ml	200 ml

If a typical dilution series (1 mM, 100 µM, 10 µM, 1 µM ...) is prepared, respective final end volumes will be 90% of the starting stock solution. For example: The content of a 10 µmol vial that has been dissolved in 10 ml of water to result in a 1 mM stock solution, yields 9 ml of each concentration level after dilution.

Interested in our experience with nucleotides?

Since we collect scientific data for most of the structures offered, we can assist you with many of your specific questions connected to nucleotide-related compounds. Since our main competence lies in cyclic nucleotide-related issues we can offer here:

- lipophilic ranking of analogues and information about membrane permeability
- phosphodiesterase hydrolysis data
- protein kinase binding, activation and inhibition data
- application references
- potential analogue pitfalls
- selection of suitable structures for respective biological systems

We invite your questions and appreciate hearing about your results and papers related to our products. Confidentiality regarding sensitive matters is, of course, assured. You are encouraged to take advantage of this service regardless whether or not you are already a customer.

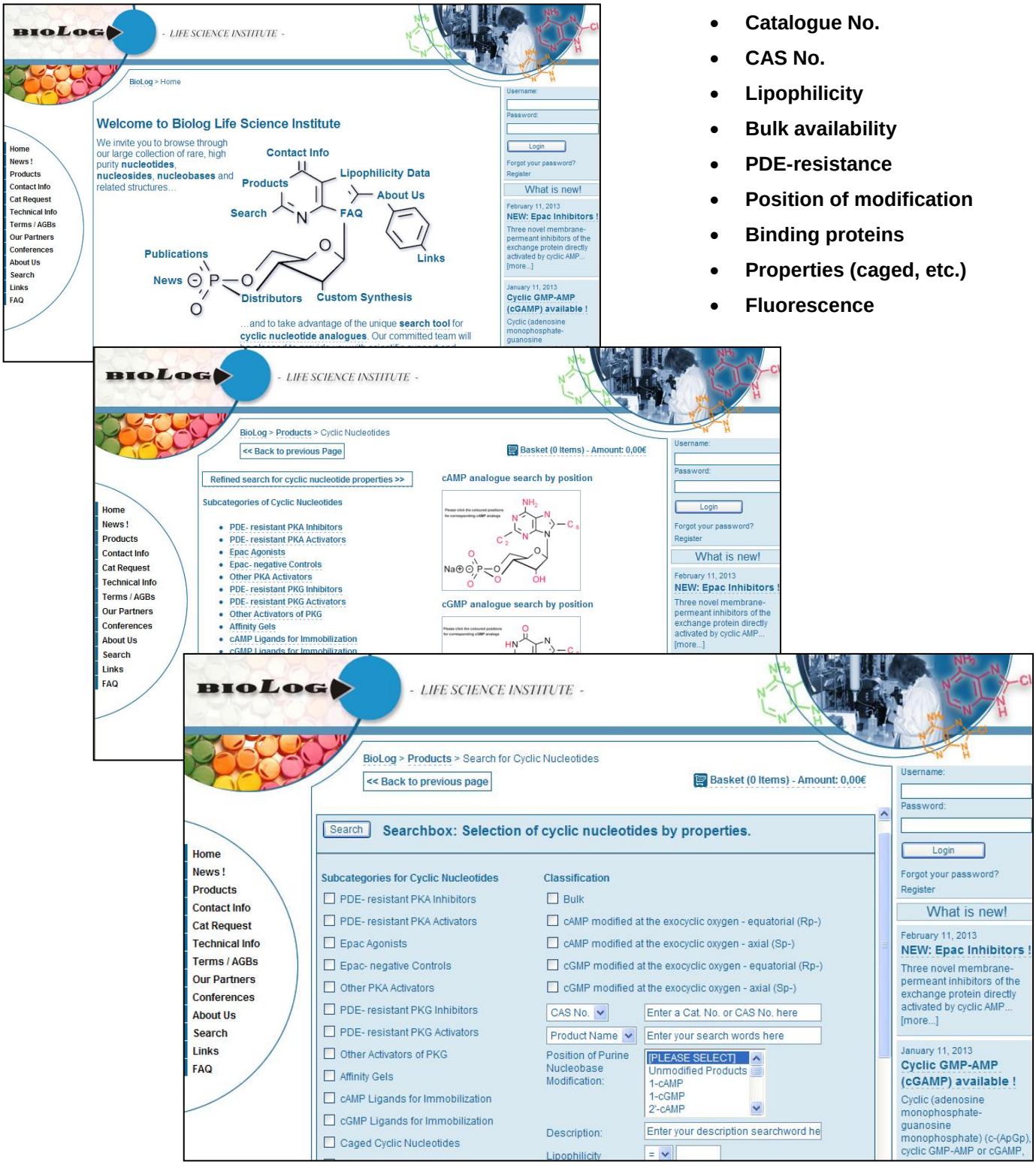
Our products are designed, developed and sold for research purposes only! They are intended for *in vitro* and nonhuman *in vivo* laboratory applications. Contents of vials are not sterile and have not been tested for endotoxins.

Please visit Biolog's website www.biolog.de

with a convenient shop system and extended search functions for cyclic nucleotide analogues

Search by:

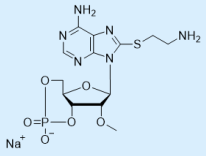
- **Name & Abbreviation**
- **Catalogue No.**
- **CAS No.**
- **Lipophilicity**
- **Bulk availability**
- **PDE-resistance**
- **Position of modification**
- **Binding proteins**
- **Properties (caged, etc.)**
- **Fluorescence**



Specific Epac Activators, negative Controls, Inhibitors and Affinity Gels

Specific Epac Activators

A 142



8- (2- Aminoethylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-AET-2'-O-Me-cAMP)

[634207-89-9]; $C_{13}H_{18}N_6O_6PS{\cdot}Na$; MW 440.4; λ_{max} 279 nm; ε 17000; sodium salt; purity > 98% HPLC.
8-AET-2'-O-Me-cAMP has only poor affinity towards protein kinases A and G and is thus suitable as a ligand in affinity chromatography of cAMP binding proteins that do not require an intact 2'-OH group, such as the exchange protein activated by cyclic AMP (Epac) and certain phosphodiesterases, and for conjugation with fluorophores, etc.. Detailed technical information available. For reference please compare: Borland et al., *Mol. Pharmacol*., **69**, 374 - 384 (2006).

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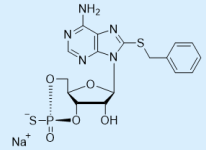
5 µmol / ~2.2 mg € 164.- (A 142 - 05)	5 x 5 µmol € 692.- (A 142 - 25)

B 046



8- Benzylthioadenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer (Sp-8-BnT-cAMPS / "S-220")

$C_{17}H_{17}N_5O_5PS_2{\cdot}Na$; MW 489.5; λ_{max} 283 nm; ε 17100; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. According to Schwede et al. (2015), Sp-8-BnT-cAMPS potently and selectively activates Epac2 over Epac1 both in vitro and in vivo (in vitro AC_{50} Epac2 = 0.1 µM (1.8 µM for cAMP) and rel. k_{max} = 7.7 (1 for cAMP)). At concentrations of 25 to 100 µM, it potentiates glucose-induced insulin secretion from primary human islets. Sp-8-BnT-cAMPS has reduced potency to activate PKA. Detailed technical information available. Reference: Schwede et al., *PLoS Biol*., **13**(1): e1002038 (2015) (Link to PLoS Biology).

Related products: Biolog also offers Sp-8-BnT-2'-O-Me-cAMPS (Cat. No. B 056 / "S-223") which has reduced potency compared to Sp-8-BnT-cAMPS, but efficiently discriminates against PKA, as well as the well-established Epac agonist 8-pCPT-2'-O-Me-cAMP (Cat. No. C 041) which selectively activates Epac1 over Epac2 (Schwede et al. 2015).

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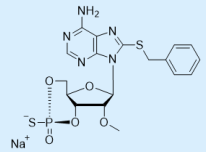
5 µmol / ~2.4 mg € 194.- (B 046 - 05)	5 x 5 µmol € 823.- (B 046 - 25)

B 056



8- Benzylthio- 2'- O- methyladenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer (Sp-8-BnT-2'-O-Me-cAMPS / "S-223")

$C_{18}H_{19}N_5O_5PS_2{\cdot}Na$; MW 503.5; λ_{max} 283 nm; ε 17100; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. According to Schwede et al. (2015), Sp-8-BnT-2'-O-Me-cAMPS is the most potent 2'-substituted activator of Epac2 that efficiently discriminates against Epac1 in vitro (AC_{50} Epac2 = 1.5 µM (1.8 µM for cAMP) and rel. k_{max} = 4.3 (1 for cAMP)). Due to the 2'-substitution it is an extremely poor PKA activator and thus allows for specific activation of Epac2 over PKA. In human osteosarcoma U2OS cell lines stably expressing Epac1 or Epac2, Sp-8-BnT-2'-O-Me-cAMPS does not induce Epac signalling at 100 µM, which may be due to inefficient cellular uptake in this biosystem. Detailed technical information available. Reference: Schwede et al., *PLoS Biol*., **13**(1): e1002038 (2015) (Link to PLoS Biology).

Related products: Biolog also offers Sp-8-BnT-cAMPS (Cat. No. B 046 / "S-220") which has increased in vitro and in vivo potency compared to Sp-8-BnT-2'-O-Me-cAMPS, but slight potency to activate PKA, as well as the well-established Epac agonist 8-pCPT-2'-O-Me-cAMP (Cat. No. C 041) which selectively activates Epac1 over Epac2 (Schwede et al. 2015).

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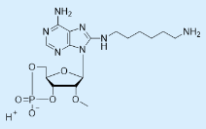
1 µmol / ~0.5 mg € 169.- (B 056 - 01)	5 x 1 µmol € 716.- (B 056 - 05)

A 099



8- (6- Aminohexylamino)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-AHA-2'-O-Me-cAMP)

$C_{17}H_{28}N_7O_6P$; MW 457.4; λ_{max} 273 nm; ε 17000; free acid; purity > 98% HPLC.
8-AHA-2'-O-Me-cAMP has only poor affinity towards protein kinases A and G and is thus suitable as a ligand in affinity chromatography of cAMP binding proteins that do not require an intact 2'-OH group, such as the exchange protein activated by cyclic AMP (Epac) and certain phosphodiesterases, and for conjugation with fluorophores, etc.. Detailed technical information available. Reference: Borland et al., *Mol. Pharmacol*., **69**, 374 - 384 (2006).

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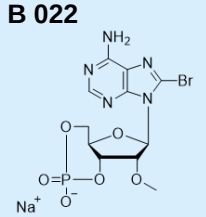
5 µmol / ~2.3 mg € 164.- (A 099 - 05)	5 x 5 µmol € 692.- (A 099 - 25)

B 022



8- Bromo- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-Br-2'-O-Me-cAMP)

[612513-13-0]; $C_{11}H_{12}BrN_5O_6P{\cdot}Na$; MW 444.1; λ_{max} 264 nm; ε 17000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Specific activator of the exchange protein activated by cyclic AMP (Epac) or cAMP-GEF, respectively, while protein kinase A is not affected. Suitable for direct comparison with common 8-Br-cAMP, which activates both, PKA and Epac. Detailed technical information and updated reference list available. References: Christensen et al., *J. Biol. Chem.*, **278**, 35394 - 35402 (2003); Traver et al., *Mol. Pharmacol*., **70**, 30 - 40 (2006).

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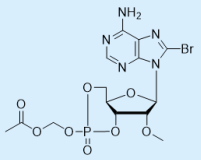
5 µmol / ~2.2 mg € 124.- (B 022 - 05)	5 x 5 µmol € 527.- (B 022 - 25)

B 028



8- Bromo- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate, acetoxymethyl ester (8-Br-2'-O-Me-cAMP-AM)

$C_{14}H_{17}BrN_5O_8P$; MW 494.2; λ_{max} 264 nm; ε 17000; purity > 97% HPLC for mixture of isomers. Extremely membrane-permeant precursor of the specific Epac agonist 8-Br-2'-O-Me-cAMP (Cat. No. B 022, above). After permeation and metabolic activation by esterases the active compound is released. Detailed technical information available. Reference: Börner et al., *Nat. Protoc.*, **6**, 427 - 438 (2011). The control reagent (PO_4-AM_3, Cat. No. P 030) is recommended.

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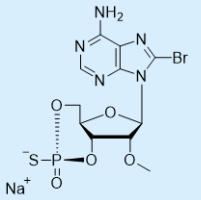
1 µmol / ~0.5 mg € 136.- (B 028 - 01)	5 x 1 µmol € 578.- (B 028 - 05)

B 031



8- Bromo- 2'- O- methyladenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer (Sp-8-Br-2'-O-Me-cAMPS)

[634208-34-7]; $C_{11}H_{12}BrN_5O_5PS{\cdot}Na$; MW 460.2; λ_{max} 264 nm; ε 17000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Hydrolysis-resistant form of 8-Br-2'-O-Me-cAMP (Cat. No. B 022, above), which is a specific membrane-permeant activator of the exchange protein directly activated by cyclic AMP (Epac) or cAMP-GEF, respectively. Detailed technical information available. References for 8-Br-2'-O-Me-cAMP: Christensen et al., *J. Biol. Chem.*, **278**, 35394 - 35402 (2003); Traver et al., *Mol. Pharmacol.*, **70**, 30 - 40 (2006).

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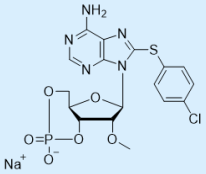
1 µmol / ~0.5 mg € 169.- (B 031 - 01)	5 x 1 µmol € 716.- (B 031 - 05)

C 041



8- (4- Chlorophenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-pCPT-2'-O-Me-cAMP / 8-CPT-2'-O-Me-cAMP / "007")

[634207-53-7]; $C_{17}H_{16}ClN_5O_6PS{\cdot}Na$; MW 507.8; λ_{max} 282 nm; ε 16000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Specific activator of the exchange protein activated by cyclic AMP (Epac) or cAMP-GEF, respectively, which does not activate protein kinase A. High lipophilicity and membrane permeability, as well as increased PDE stability. Detailed technical information and updated references available. Metabolites are offered as well (Cat. No. C 069, Cat. No. C 070, inquire). References: Enserink et al., *Nature Cell Biol.*, **4**, 901 - 906 (2002); Kang et al., *J. Biol. Chem.*, **278**, 8279 - 8285 (2003); Christensen et al., *J. Biol. Chem.*, **278**, 35394 - 35402 (2003).

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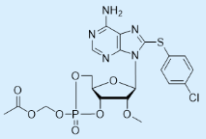
5 µmol / ~2.5 mg € 136.- (C 041 - 05)	5 x 5 µmol € 578.- (C 041 - 25)	**Inquiries for bulk quantities welcome!**

C 051



8- (4- Chlorophenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate, acetoxymethyl ester (8-pCPT-2'-O-Me-cAMP-AM / 8-CPT-2'-O-Me-cAMP-AM)

[1152197-23-3]; $C_{20}H_{21}ClN_5O_8PS$; MW 557.9; λ_{max} 282 nm; ε 16000; purity > 97% HPLC for mixture of isomers. Extremely membrane-permeant precursor of the specific Epac agonist 8-CPT-2'-O-Me-cAMP (Cat. No. C 041). After permeation and metabolic activation by esterases the active compound is released. Detailed technical information available. References: Vliem et al., *ChemBioChem*, **9**, 2052 - 2054 (2008); Chepurny et al., *J. Biol. Chem.*, **284**, 10728 - 10736 (2009); Chepurny et al., *Am. J.Physiol.*, **298**, E622 - E633 (2010).
Biolog also offers phosphate tris(acetoxymethyl)ester (PO_4-AM_3, Cat. No. P 030) which is recommended as control reagent in nucleotide-AM ester applications.

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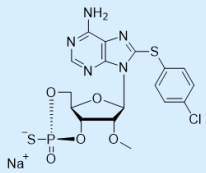
1 µmol / ~0.6 mg € 136.- (C 051 - 01)	5 x 1 µmol € 578.- (C 051 - 05)

C 052



8- (4- Chlorophenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer (Sp-8-pCPT-2'-O-Me-cAMPS / Sp-8-CPT-2'-O-Me-cAMPS)

[634208-37-0]; $C_{17}H_{16}ClN_5O_5PS_2{\cdot}Na$; MW 523.9; λ_{max} 282 nm; ε 16000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Hydrolysis-resistant form of 8-pCPT-2'-O-Me-cAMP (Cat. No. C 041), a specific activator of the exchange protein directly activated by cyclic AMP (Epac) or cAMP-GEF, respectively. The compound does not activate protein kinase A, has high lipophilicity and membrane permeability and is not metabolized by phosphodiesterases. Detailed technical information available. References: Laxman et al., *Proc. Natl. Acad. Sci. USA*, **103**, 19194 - 19199 (2006); Ouyang et al., *Proc. Natl. Acad. Sci. USA*, **105**, 11993 - 11997 (2008).

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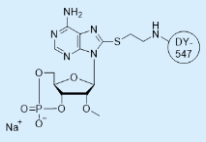
1 µmol / ~0.5 mg € 169.- (C 052 - 01)	5 x 1 µmol € 716.- (C 052 - 05)

D 089



8- (2- [DY-547]- aminoethylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-[DY-547]-AET-2'-O-Me-cAMP)

$C_{43}H_{51}N_8O_{13}PS_3{\cdot}Na_2$; MW 1061.1; λ_{max} 559 nm; ε 150000 (EtOH); sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Fluorescent activator of the exchange protein directly activated by cyclic AMP (Epac) or cAMP-GEF, respectively, which does not activate PKA (λ_{exc} 557 nm, λ_{em} 574 nm). Detailed technical information available.

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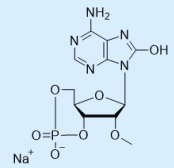
0.1 µmol / ~0.1 mg € 185.- (D 089 - 001)	5 x 0.1 µmol € 786.- (D 089 - 005)

H 013



8- Hydroxy- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-OH-2'-O-Me-cAMP)

$C_{11}H_{13}N_5O_7P{\cdot}Na$; MW 381.2; λ_{max} 268 nm; ε 11000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Specific activator of the exchange protein activated by cyclic AMP (Epac) or cAMP-GEF, respectively, which does not activate protein kinase A. Due to its low lipophilicity and membrane permeability, 8-OH-2'-O-Me-cAMP can be used in patch clamp applications. Detailed technical information available.

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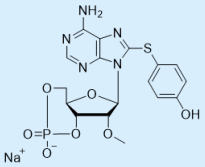
5 µmol / ~1.9 mg € 136.- (H 013 - 05)	5 x 5 µmol € 578.- (H 013 - 25)

H 010



8- (4- Hydroxyphenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-pHPT-2'-O-Me-cAMP)

[612513-15-2]; $C_{17}H_{17}N_5O_7PS{\cdot}Na$; MW 489.4; λ_{max} 282 nm; ε 16000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Specific activator of the exchange protein activated by cyclic AMP (Epac) or cAMP-GEF, respectively, which does not activate protein kinase A. High lipophilicity and membrane permeability, as well as increased PDE stability. Detailed technical information and updated references available. References: Christensen et al., *J. Biol. Chem.*, **278**, 35394 - 35402 (2003); Holz et al., *J. Physiol.*, **577**, 5 - 15 (2006).

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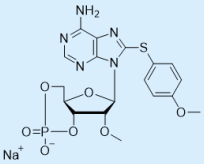
5 µmol / ~2.4 mg € 136.- (H 010 - 05)	5 x 5 µmol € 578.- (H 010 - 25)

M 034



8- (4- Methoxyphenylthio)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-pMeOPT-2'-O-Me-cAMP)

[612513-16-3]; $C_{18}H_{19}N_5O_7PS{\cdot}Na$; MW 503.4; λ_{max} 282 nm; ε 16000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Very potent and specific activator of the exchange protein activated by cyclic AMP (Epac) or cAMP-GEF, respectively, which does not activate protein kinase A. High lipophilicity and membrane permeability, as well as increased PDE stability. Detailed technical information and updated references available. A potential metabolite of 8-pMeOPT-2'-O-Me-cAMP is offered as well (Cat. No. M 061, inquire). References: Christensen et al., *J. Biol. Chem.*, **278**, 35394 - 35402 (2003); Holz et al., *J. Physiol.*, **577**, 5 - 15 (2006).

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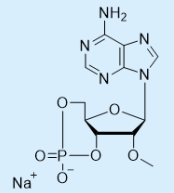
5 µmol / ~2.5 mg € 136.- (M 034 - 05)	5 x 5 µmol € 578.- (M 034 - 25)

M 050



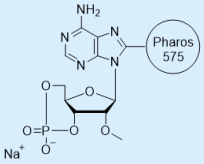
2'- O- Methyladenosine- 3', 5'- cyclic monophosphate (2'-O-Me-cAMP)

[40269-29-2]; $C_{11}H_{13}N_5O_6P{\cdot}Na$; MW 365.2; λ_{max} 259 nm; ε 15000; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Relatively polar analogue of cyclic AMP which does not activate protein kinase A. Suitable for Epac activation by patch clamp application techniques and for receptor mapping studies. The structurally related cGMP-based analogue 2'-O-Me-cGMP is offered as well (Cat. No. M 036). Detailed technical information available. Reference: Kang et. al., *J. Physiol.*, **573**, 595 - 609 (2006).

5 µmol / ~1.8 mg € 80.- (M 050 - 05)	5 x 5 µmol € 338.- (M 050 - 25)	**Inquiries for bulk quantities welcome!**

P 021

Membrane-permeant !



8- [Pharos-575]- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate (8-[φ-575]-2'-O-Me-cAMP)

Sodium salt; purity > 98% HPLC; λ_{max} 575 nm; ε 20960. For other salt forms please inquire.
The EPAC activator 2'-O-Me-cAMP connected to the relatively small Pharos 575 dye (λ_{exc} 577 nm, λ_{em} 605 nm). The fluorophore can be excited e.g. by a Kr/Ar-laser. Due to its high lipophilicity and bright red fluorescence, 8-[φ-575]-2'-O-Me-cAMP is especially suitable for studies with intact cells. Detailed technical information available. For reference compare: Moll et al., *BMC Biochemistry*, **9**:18 (2008).

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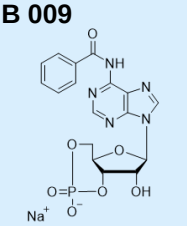
0.1 µmol / ~74 µg € 238.- (P 021 - 001)	5 x 0.1 µmol € 998.- (P 021 - 005)

PKA- selective agonists that do not activate Epac & Epac- negative Controls

B 009

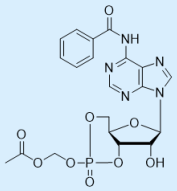


N^6- Benzoyladenosine- 3', 5'- cyclic monophosphate (6-Bnz-cAMP)

[30275-80-0]; $C_{17}H_{15}N_5O_7P{\cdot}Na$; MW 455.3; λ_{max} 279 nm; ε 19700; sodium salt; purity > 98% HPLC.
For other salt forms or metabolites of 6-Bnz-cAMP please inquire. Site-selective and membrane-permeant activator of cAMP-dependent protein kinase. 6-Bnz-cAMP does not activate Epac and thus can be used as an Epac-negative control. For more details on site selectivity please see inquire. Detailed technical information and updated reference list available. References: Christensen et al., *J. Biol. Chem.*, **278**, 35394 - 35402 (2003); Bos, *Trends Biochem. Sci.*, **31**, 680 - 686 (2006).

10 µmol / ~4.6 mg € 80.- (B 009 - 10)	5 x 10 µmol € 338.- (B 009 - 50)	**Inquiries for bulk quantities welcome!**

B 079



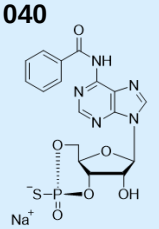
N^6- Benzoyladenosine- 3', 5'- cyclic monophosphate, acetoxymethyl ester (6-Bnz-cAMP-AM)

$C_{20}H_{20}N_5O_9P$; MW 505.4; λ_{max} 279 nm; ε 17000; purity > 97% HPLC for mixture of isomers.
Extremely membrane-permeant precursor of the specific PKA agonist 6-Bnz-cAMP (Cat. No. B 009, above). After permeation and metabolic activation by esterases the active compound is released. 6-Bnz-cAMP-AM does not activate Epac and thus can be used as an Epac-negative control. Reference: Leech et al., *Islets*, **2**, 72 - 81 (2010).

Control reagent for nucleotide AM-ester applications: PO_4-AM_3, Cat. No. P 030

1 µmol / ~0.5 mg € 101.- (B 079 - 01)	5 x 1 µmol € 430.- (B 079 - 05)

B 040

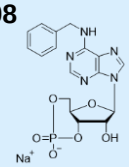


N^6- Benzoyladenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer (Sp-6-Bnz-cAMPS)

[152218-18-3]; $C_{17}H_{15}N_5O_6PS{\cdot}Na$; MW 471.4; λ_{max} 279 nm; ε 17000; sodium salt; purity > 98% HPLC.
Site-selective, PDE-resistant and membrane-permeant activator of cAMP-dependent protein kinase. Sp-6-Bnz-cAMPS does not activate Epac and thus can be used as an Epac-negative control. For more details on site selectivity please inquire. Detailed technical information available. Reference: Lim et al., *Neurosci. Lett*., **479**, 13 - 17 (2010).

5 µmol / ~2.4 mg € 164.- (B 040 - 05)	5 x 5 µmol € 692.- (B 040 - 25)

B 008



N^6- Benzyladenosine- 3', 5'- cyclic monophosphate (6-Bn-cAMP)

[32115-08-5]; $C_{17}H_{17}N_5O_6P{\cdot}Na$; MW 441.3; λ_{max} 268 nm; ε 20500; sodium salt; purity > 98% HPLC.
Site-selective activator of cAMP-dependent protein kinase which is considered not to activate Epac. Increased hydrolytic stability against PDE, esterases, amidases and considerably higher membrane permeability compared to cAMP. Detailed technical information and updated reference list available. Reference: Pepe et al., *Cancer Res*., **51**, 6263 - 6267 (1991).

10 µmol / ~4.4 mg € 99.- (B 008 - 10)	5 x 10 µmol € 420.- (B 008 - 50)

B 037

8- Bromo- 2'- O- methylguanosine- 3', 5'- cyclic monophosphate (8-Br-2'-O-Me-cGMP)

$C_{11}H_{12}BrN_5O_7P{\cdot}Na$; MW 460.1; λ_{max} 260 nm; ε 15000; sodium salt; purity > 98% HPLC. For other salt forms please inquire. Analogue of cyclic GMP which does not activate both, protein kinase G and Epac. 8-Br-2'-O-Me-cGMP can be used as an inactive control versus 8-Br-cGMP (Cat. No. B 004). Detailed technical information available.

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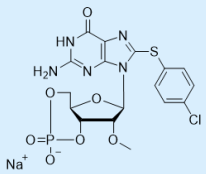
5 µmol / ~2.3 mg € 98.- (B 037 - 05)	5 x 5 µmol € 416.- (B 037 - 25)

C 048



8- (4- Chlorophenylthio)- 2'- O- methylguanosine- 3', 5'- cyclic monophosphate (8-pCPT-2'-O-Me-cGMP)

[625112-42-7]; $C_{17}H_{16}ClN_5O_7PS{\cdot}Na$; MW 523.8; λ_{max} 276 nm; ε 21500; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. The membrane-permeant 8-pCPT-2'-O-Me-cGMP neither activate protein kinase G nor Epac and can thus be used as a control. Characterized by high lipophilicity and membrane permeability, as well as increased PDE stability. Detailed technical information available. Reference: Haag et al., *Naunyn-Schmiedeberg's Arch. Pharmacol.*, **378**, 617 - 630 (2008).

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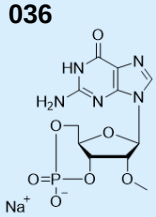
5 µmol / ~2.6 mg € 136.- (C 048 - 05)	5 x 5 µmol € 578.- (C 048 - 25)

M 036



2'- O- Methylguanosine- 3', 5'- cyclic monophosphate (2'-O-Me-cGMP)

[949909-73-3]; $C_{11}H_{13}N_5O_7P{\cdot}Na$; MW 381.2; λ_{max} 252 nm; ε 13500; sodium salt; purity > 98% HPLC.
For other salt forms please inquire. Relatively polar analogue of cyclic GMP which activates neither protein kinase G nor Epac. 2'-O-Me-cGMP can be used as an inactive control in patch clamp applications. Also suitable for receptor mapping studies. The structurally related cAMP-based analogue 2'-O-Me-cAMP is offered as well (Cat. No. M 050). Detailed technical information available. Reference: Kang et. al., *J. Physiol.*, **573**, 595 - 609 (2006).

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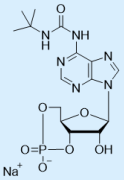
5 µmol / ~1.9 mg € 83.- (M 036 - 05)	5 x 5 µmol € 353.- (M 036 - 25)

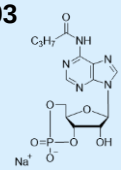
M 012

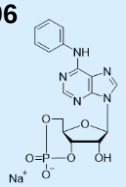


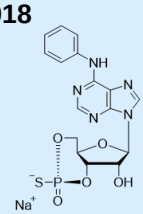
N^6- Mono- tert.- butylcarbamoyladenosine- 3', 5'- cyclic monophosphate (6-MBC-cAMP)

[84433-46-5]; $C_{15}H_{20}N_6O_7P{\cdot}Na$; MW 450.3; λ_{max} 268 nm; ε 23700; sodium salt; purity > 98% HPLC. For other salt forms please inquire. Site-selective activator of protein kinase A (cyclic AMP agonist) strongly preferring the A site of cAK II. Together with e.g. Sp-5,6-DCl-cBIMPS (Cat. No. D 014) selective stimulation of type II can be achieved. 6-MBC-cAMP is considered not to activate Epac. Detailed technical information and updated reference list available. References: Maronde et al., *J. Pineal Res*., **27**, 170 - 182 (1999); Fricke et al., *Endocrinology*, **145**, 4940 - 4947 (2004).

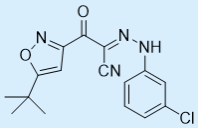
5 µmol / ~2.3 mg € 65.- (M 012 - 05)	5 x 5 µmol € 277.- (M 012 - 25)

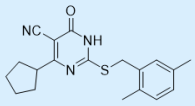
M 003 	**N^6- Monobutyryladenosine- 3', 5'- cyclic monophosphate (6-MB-cAMP)** [70253-67-7]; $C_{14}H_{17}N_5O_7P{\cdot}Na$; MW 421.3; λ_{max} 273 nm; ε 19000; sodium salt; purity > 97% HPLC. For other salt forms or metabolites please inquire. Membrane-permeant, site-selective activator of protein kinase A (cyclic AMP agonist). 6-MB-cAMP does not activate Epac and thus can be used as an Epac-negative control. Detailed technical information and selected references available. Reference: Kopperud et al., *FEBS Lett*., **546**, 121 - 126 (2003).		
50 µmol / ~21 mg € 62.- (M 003 - 50)		5 x 50 µmol € 264.- (M 003 - 250)	

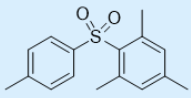
P 006 	**N^6- Phenyladenosine- 3', 5'- cyclic monophosphate (6-Phe-cAMP)** [34051-30-4]; $C_{16}H_{15}N_5O_6P{\cdot}Na$; MW 427.3; λ_{max} 288 nm; ε 20800; sodium salt; purity > 98% HPLC. Potent site-selective and highly membrane-permeant activator of protein kinase A. 6-Phe-cAMP is considered not to activate Epac and thus can be used as an Epac-negative control. For more details on site selectivity please see p. 14. Detailed technical information and updated reference list available. Reference: Kloss et al., *Mol. Pharmacol*., **65**, 1440 - 1451 (2004).		
5 µmol / ~2.1 mg € 60.- (P 006 - 05)		5 x 5 µmol € 254.- (P 006 - 25)	

P 018 	**N^6- Phenyladenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer (Sp-6-Phe-cAMPS)** [169335-92-6]; $C_{16}H_{15}N_5O_5PS{\cdot}Na$; MW 443.4; λ_{max} 288 nm; ε 20800; sodium salt; purity > 98% HPLC. Potent site-selective, highly membrane-permeant and PDE-resistant activator of protein kinase A. Sp-6-Phe-cAMPS does not activate Epac and thus can be used as an Epac-negative control. For more details on site selectivity please inquire. Detailed technical information available. References: Gjertsen et al., *J. Biol. Chem*., **270**, 20599 - 20607 (1995); Ouyang et al., *Proc. Natl. Acad. Sci. USA*, **105**, 11993 - 11997 (2008).		
5 µmol / ~2.2 mg € 142.- (P 018 - 05)		5 x 5 µmol € 600.- (P 018 - 25)	

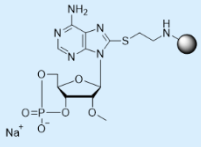
Selective Epac Inhibitors

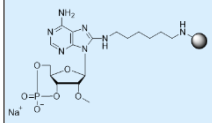
B 133 	**3- [5- (tert.- Butyl)isoxazol- 3- yl]- 2- [2- (3- chlorophenyl)hydrazono]- 3- oxopropanenitrile (ESI-09)** [263707-16-0]; $C_{16}H_{15}ClN_4O_2$; MW 330.8; λ_{max} 384 nm; ε 25300; purity > 95% HPLC. Membrane-permeant inhibitor of Epac 1 and Epac 2. Detailed technical information available. Reference: Almahariq et al., *Mol. Pharmacol*., **83**, 122 - 128 (2013).		
5 µmol / ~1.7 mg € 128.- (B 133 - 05)		5 x 5 µmol € 545.- (B 133 - 25)	

C 136 	**4- Cyclopentyl- 2- (2, 5- dimethylbenzylsulfanyl)- 6- oxo- 1, 6- dihydropyrimidine- 5- carbonitrile (HJC0197)** [1383539-73-8]; $C_{19}H_{21}N_3OS$; MW 339.5; λ_{max} 304 nm; ε 14700; purity > 95% HPLC. Membrane-permeant inhibitor of Epac 1 and Epac 2. Detailed technical information available. Reference: Chen et. al., *Bioorg. Med. Chem. Lett.*, **22**, 4038 - 4043 (2012).		
5 µmol / ~1.7 mg € 128.- (C 136 - 05)		5 x 5 µmol € 545.- (C 136 - 25)	

M 092 	**4- Methylphenyl- 2, 4, 6- trimethylphenylsulfone (ESI-05)** [5184-64-5]; $C_{16}H_{18}O_2S$; MW 274.4; λ_{max} 244 nm; ε 19000; purity > 95% HPLC. Membrane-permeant selective inhibitor of Epac 2. Detailed technical information available. Reference: Tsalkova et al., *Proc. Natl. Acad. Sci. USA*, **109**, 18613 - 18618 (2012).		
5 µmol / ~1.4 mg € 128.- (M 092 - 05)		5 x 5 µmol € 545.- (M 092 - 25)	

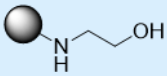
Epac Affinity Gels

A 195 	**8- (2- Aminoethylthio)- 2'-O- methyladenosine- 3', 5'- cyclic monophosphate; immobilized on agarose gel (8-AET-2'-O-Me-cAMP-Agarose)** The second messenger cyclic AMP with a methylated ribose 2'-hydroxyl group immobilized on agarose by an aminoethylthio spacer attached to position 8 of the ligand. Considered to be suitable for affinity chromatography of various cAMP-responsive proteins, especially those which tolerate modification of the ribose 2'-hydroxyl group, such as the exchange protein activated by cyclic AMP (Epac) and certain phosphodiesterases. Detailed technical information available. Also available as free beads (without column). Protected by patent n° EP 02077219.0 and foreign equivalents, exclusively licensed to BIOLOG LSI for research purposes only		
Columns:	0.6 ml € 186.- (A 195 - 06)	2.5 ml € 583.- (A 195 - 25)	6 ml € 1,134.- (A 195 - 60)

A 057 	**8- (6- Aminohexylamino)- 2'- O- methyladenosine- 3', 5'- cyclic monophosphate; immobilized on agarose gel (8-AHA-2'-O-Me-cAMP-Agarose)** cAMP with a methylated ribose 2'-hydroxy group immobilized on agarose by an aminohexylamino spacer attached to position 8 of the ligand. Suitable for affinity chromatography of various cAMP-responsive proteins, especially those which tolerate modification of the ribose 2'-hydroxy group, such as the exchange protein activated by cyclic AMP (Epac) and certain phosphodiesterases. Detailed technical information available. Reference: Borland et al., *Mol. Pharmacol*., **69**, 374 - 384 (2006). Also available as free beads (without column). Protected by patent n° EP 02077219.0 and foreign equivalents, exclusively licensed to BIOLOG LSI for research purposes only		
Columns:	0.6 ml € 186.- (A 057 - 06)	2.5 ml € 583.- (A 057 - 25)	6 ml € 1,134.- (A 057 - 60)

Inquire	**Special Epac-related analogues not listed** The product line of Epac-specific modulators will be extended. For structures not yet listed please inquire. An updated list of products will be published on our website (www.biolog.de).

Control for Affinity Chromatography Gels

E 010 	**Ethanolamine; immobilized on agarose gel (EtOH-NH-Agarose)** Agarose gel without nucleotide ligands, as negative control in affinity chromatography experiments. This agarose matrix is identical to the material used for the synthesis of the affinity gels listed above. The reactive groups on the bead surface normally used to immobilize the functionalized nucleotide, have been deactivated with ethanolamine. Reference: Antl et al., *Blood*, **109**, 552 - 559 (2007); Hammerschmidt et al., *PLoS One* **7**(7): e39848 (2012).		
Columns:	0.6 ml € 82.- (E 010 - 06)	2.5 ml € 255.- (E 010 - 25)	6 ml € 513.- (E 010 - 60)

Alphabetical listing of products and abbreviations

We appreciate your interest in our product line. Please take a moment to review the following notes:

- **Orders** can be placed at our online shop, but are welcome by phone, e-mail, fax or regular mail as well, of course. Customers from EC countries are requested to submit the European tax registration number of their institution along with their order.

- **Shipping** of your order will be prepared as soon as possible. Unless otherwise instructed, items requiring refrigeration may not be shipped on Thursday or Friday to avoid weekend storage under unsuitable conditions.

- **Prices** are shown in Euro and do not include taxes or foreign duties (if applicable). There are no packing or transport costs for air mail delivery, however, courier service and dry ice shipments (recommended for e.g. all triphosphates & diphosphates) will be extra charged. We reserve the right to change prices without prior written notice, however, products will not be shipped at an increased price without authorization from the customer.

- **Courier** costs depend on destination: approx. € 35.- for customers in Germany, € 50.- – € 150.- within Europe, and € 100.- – € 350.- for the rest of the world. Please check every arriving parcel for any obvious damage before signing the receipt, otherwise compensation for broken vials is not possible.

- **Invoices** are payable net 30 days by bank transfer; no deductions accepted. European customers are urged to use the SEPA payment system. Corresponding bank details (BIC and IBAN) are shown on all our paper work.

- **Bulk:** Many of our products can be supplied in larger sizes. Favourable quotations for bulk quantities or discounts on purchase of multiple vials are available upon request.

- **Discounts** can be granted for amounts exceeding catalogue sizes, and for customers identified as permanent buyers. Standing orders with favourable conditions are possible upon request.

- **Support** for our products is provided in form of corresponding technical information that accompanies every product. Additional and updated data can be found on our website (www.biolog.de), especially regarding published references, lipophilicity and specificity. We try hard to support you with all background knowledge available to us, so please contact us by e-mail (service@biolog.de) in case you have special questions, or if you would like to suggest a new product.

- **Feed-back** on performance of our products is very much appreciated, be it positive or negative. It encourages us, helps us to improve, and leads to better and more qualified service for our customers. Also, we would like to hear about your new papers with our products, in order to have the citation included in the corresponding technical information.

- **Custom syntheses** of many structures not listed in this catalogue are offered. Please contact us with your research needs, and be sure to specify purity, salt form and amounts necessary.

- **Quality:** If you are not satisfied with our product, please contact us. Products may not be returned or an invoice annulled without prior written approval from BIOLOG. We cannot be held responsible for damage to material because of improper storage or handling after receipt.

- **Safety:** All products in this catalogue are sold for research purposes only and are **not** intended for human, drug, food additive, clinical, or household use. Only qualified professionals and trained laboratory staff familiar with their potential hazards and trained in good laboratory practices should handle them. Some of the products could be toxic or hazardous compounds. When available, information pertaining to the potential hazards is provided. However, the absence of a warning must **not** be interpreted as an indicator of safety. Material Safety Data Sheets (MSDS) are available upon request.

Terms and Conditions of Sale and Synthesis

Last updated: May 20, 2017

I. Conclusion of Contract

1. The following conditions apply and become an integral part of all purchase or other orders for synthesis of products confirmed by us, Biolog Life Science Institute, and apply to all our quotations. They are deemed accepted and acknowledged by our clients in placing an order with us or in taking possession of the delivery. Divergent conditions of our clients whose application is not explicitly confirmed in writing by us are not binding even if there was no expressed contradiction.
2. All our quotations are subject to change. The conclusion of the contract can be regarded final only after the client has received our order confirmation. Oral agreements, amendments or additions to the contract are binding only if confirmed by us in writing.
3. We retain ownership, copyright and inventor's rights in all quotations, cost estimates, compound lists, structures and other documents. Quotations and connected documentation must not be disclosed to third parties unless our prior authorization has been obtained.
4. The client accepts that personal data are recorded by us within the scope of the provisions of the BDSG (German Federal Data Protection Law).

II. Prices and Payment

1. Prices shown on the web and in the printed catalogue are in Euro. For price information and our acceptance of other currencies such as US Dollar, please inquire.
2. Prices shall be understood without value added tax. Shipping costs are extra charged (approx. Euro 30.00 within Germany; approx. Euro 40.00 - 100.00 within Europe, and for the rest of the world according to destination). Please note, that some products, e.g. all triphosphates, require courier transport with blue or dry ice in order to maintain their original high quality and purity. This will lead to extra costs, please inquire for details. Airmail postal service may be available for some destinations without any additional costs.
3. We are entitled to charge our clients additionally to the contract price all increases in expenses accrued in connection with the supply or service provided such increases become effective after conclusion of the contract. This right is independent from the cause of increase as there are legal regulations or other regulations or factual reasons. Expenses which we debit to our clients are especially export and import charges as custom duties, price-adjustment levies and taxes, storage charges, insurance premiums and similar costs which are out of the scope of our direct influence.
4. Along with the products ordered you will receive our invoice which is due net 30 days. Payment becomes overdue on the 31st day after invoice date. Invoices should be paid by bank transfer free of expenses for us. Bank details are given on the invoice.
5. Without prejudice to any more extensive rights we are entitled in case of default of payment to demand interest on arrears of 8 % above the current discount rate published by the Deutsche Bundesbank.
6. A set-off or other retention of payment in view of counter claims of the client is admissible only if the counter-claims have been acknowledged by us or the claims have been finally determined by court order.
7. We are entitled to demand, in our choice, the provision of security through letter of credit or other securities such as prepayment. Should the client not comply with this demand within ten days, we have the rights, after expiry of an additional term of 5 days to repudiate the contract.

III. Terms of Delivery

1. We are not obliged to comply with the agreed delivery term until the client has fulfilled his contractual obligations or duties imposed on him in particular the stipulated financial commitments. The term of delivery shall be complied with if the products to be delivered have left our premises or readiness for despatch has been announced.
2. The term of delivery shall be adequately extended if the completion or delivery of the products is delayed by strikes, lockouts or other obstacles beyond our control (force majeure). We shall notify the client about such circumstances without undue delay.
3. Delivery of products which are not produced by us is subject to obtaining punctual and complete supply ourselves.
4. Goods may not be returned to us except with our prior permission. Goods can only be accepted for return if they are unopened and in good condition. Transport costs for returned goods are for the purchaser's account. Any returned items may be subject to a processing fee.

IV. Transition of Risk

1. We despatch products on account and risk of our clients. The risk shall pass to the client, even with freight prepaid shipments, at the time the products are handed over to the carrier or with commencement of transit by ourselves or by acceptance by the persons instructed by the client. We undertake to assign existing rights and remedies against the carrier on first simple demand and unconditional payment of the contract price by the client.
2. By unconditional acceptance of the products by the carrier or by the person instructed by the client all subsequent claims regarding the external condition (packing, leakage etc.) are precluded.
3. Even if the delivered products show considerable faults, they have to be accepted by the client, however, without prejudice for subsequent guaranty claims concerning the product. The client must, however, examine the delivery in every respect for any lack of conformity with the contract and shall give notice of any lack of conformity with the contract or will be excluded with all subsequent claims.
4. In the event the client defaults in the acceptance of the products or providing security, we are entitled, without prejudice to our rights for repudiation of the contract, to demand a lump sum indemnity of 5 % of the total delivery value. We as well as the client are not precluded from claiming and proving a higher or lower damage.

V. Retention of Title

1. We retain the right of property in the products delivered until all our present or accessory claims against the client, irrespective of their cause, are settled. In acceptance of drafts or of bills of exchange or in assuming the liability under a bill of exchange by acceptance or issue of a bill of exchange the title in the products does not pass to the client before the draft or bill of exchange has been finally honoured and it has been ascertained that no claims can be lodged against us based upon the documentary credits. Inserting claims in a current account as well as acknowledgment of a balance does not affect the retention of title.
2. The client is authorized to use the products supplied for research purposes only if not otherwise confirmed in writing. He is also entitled to mix or synthesize with the products at his own risk. The title in our products is extended to new products synthesized by our client. In case our title in the products is extinguished by combination, mixture up or incorporation of other products the client herewith transfers title in the new synthesized products to us which is held as security for all claims as per para. 1 above. The products we obtained title in are stored free of charge by the client without giving any cause of action against us in view of the mixing up, the synthesis or the storage of the products.
3. In any case, the client agrees that any and all intellectual property or other rights, know-how, and methods relating to the synthesis or purchase contract remain our sole property.

VI. Guaranty and Liability

1. We do not assume liability for oral advices of any kind - which are non-binding in any event - to the client. Any advice, oral or written, regarding the area of application of our products does not dispense the client from a self-responsible examination regarding the qualification of the products for the intended purposes or methods as well as of any infringement with issued or pending intellectual property rights belonging to third parties.
2. Our products are for laboratory research use only if not otherwise confirmed in writing. They must not be used with human subjects or for clinical diagnosis or therapeutic use in humans or animals, including, but not limited to, commercial purposes, *in vitro* diagnostic purposes, ex vivo or in vivo therapeutic purposes, investigational use, in foods, drugs, devices or cosmetics of any kind, or for consumption by or use in connection with or administration or application to humans or animals.
3. Our products are not sterile and are not regularly checked for endotoxins. Products carrying a charge are essentially desalted by common standard techniques for nucleotides. Please be aware, that efficacy of all known desalting methods is limited and dependent on properties of the particular product. Final preparations of products may therefore contain a minor residual salt content.
4. The product descriptions on our web site and in our catalogue are accurate to the best of our knowledge. Since research applications are subjected to variable influences beyond our control, the products are offered without performance warranty, expressed or implied. In any case we reserve the right, from time to time, to modify composition and purity, in response to changes in the market conditions, raw material supply or other factors. Many products are new and experimental and have not been tested for toxicity. PLEASE NOTE THAT THE ABSENCE OF A WARNING STATEMENT DOES NOT IMPLY THAT THE PRODUCT IS NOT HAZARDOUS. Research products should be used only by qualified investigators or by technically trained personnel working under the direct supervision of such investigators. It is the investigator's responsibility to ensure the safe handling of all products.
5. If any research product fails to meet the physical criteria ascribed to it on the catalogue, our web site or by any other analysis or description issued by us in writing, we will, after validating the deficiency, at the option of the client, either replace the deficient product in kind or will issue a Euro credit equivalent to the purchase price of the deficient product.
6. We will not be liable under any legal theory (including but not limited to contract, negligence, strict liability in tort or warranty of any kind) for any indirect, special, incidental, consequential or exemplary damages (including but not limited to lost profits), even if we had notice of the possibility of such damages. We shall not be liable for any loss, damage or penalty as a result of any delay in or failure to deliver or otherwise perform hereunder. In any event the extent of our liability is restricted to the damage to the product itself.
7. If the fault or omission of the ascribed quality is caused by the delivery or performance of a sub-supplier our liability is restricted to an assignment of our rights and remedies we have against the sub-supplier. We undertake to assign these rights and remedies on first simple demand. If the client is not able to recover from the sub-supplier, he is entitled to keep us liable according para. VI. 4. in a subsidiary way.
8. Refund, replacement or any other claims is conditioned on client giving written notice to us within thirty (30) days after arrival of the products at its destination. Failure of client to give said notice within said thirty (30) days shall constitute a waiver by the client of all claims hereunder with respect to said material. Our liability under VI. 9. below remains unaffected.
9. In any event, any claim of the client against us for, but not limited to refund, replacement, remuneration for consequential damages or otherwise is excluded under the statute of limitations after one year after arrival of the products at its destination. Our liability under VI. 9. below remains unaffected.
10. Our liability for intention or gross negligence, for an expressed warranty, for the violation of an obligation which was of absolute material importance for the intended purpose of the contract, under the statute for the liability for defect products, and for personal injury or death remains unaffected. In cases of gross negligence and in cases of our failure to fulfil an obligation which was of absolute material importance for the intended purpose of the contract we are liable only for the immediate and foreseeable damage.
11. As our products are delivered to the clients for research purposes only, the client shall indemnify us, without prejudice to our continuing legal rights and waiving any defence of limitation, without limit against any and all claims of third parties which are brought against us on the grounds of product liability, to the extent the claim is based on circumstances which were caused after risk passed to the client.

VII. Legal Clauses

1. The sole and exclusive place of performance for all contractual or other obligations under the contract as well as the sole and exclusive place of jurisdiction shall be Bremen for both parties.
2. Any dispute between the parties shall be governed by German law.
3. In case one of the above stipulations has been proved invalid the validity of the remaining provisions remain unaffected.

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