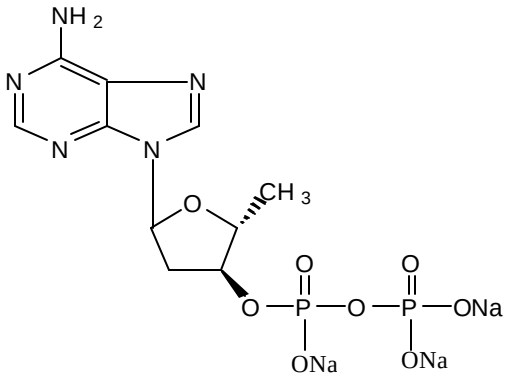
3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone (800) 325-5832 (314) 771-5765
Fax (314) 286-7828
email: techserv@sial.com
sigma-aldrich.com

ProductInformation

2′,5′-Dideoxyadenosine 3′-diphosphate
Trisodium salt

Product Number **D 0814**
Storage Temperature –20 °C

CAS #: 162554-03-2
Synonyms: 2′,5′-dd-3′ ADP; 2′,5′-dideoxy-3′-ADP



Product Description

Molecular Formula: $C_{10}H_9N_5O_8P_2 \bullet 3Na$
Molecular Weight: 458.1 (anhydrous)
Supplied as off-white solid
Purity: 90% (HPLC). It contains 5% of 2′5′-dideoxy-3′AMP.

Adenylyl cyclase (AC) is a family of membrane bound enzymes composed of alternating membrane and cytoplasmic domains. Two major cytoplasmic domains, C_{1a} and C_{2a} , form the catalytic core of the enzyme, that contains the primary binding sites for activators of AC. AC catalyzes the formation of 3′,5′- cAMP from 5′ATP and is regulated by numerous neurotransmitters and hormones via cell surface receptors and guanine nucleotide-dependent regulatory proteins (G-proteins).[1]

The inhibition of AC occurs via the 3′-nucleotide site on adenylyl cyclase, named the P-site because of the requirement for a purine moiety. Inhibition through P-site is a property of all known isoforms of mammalian AC.[2,3] P-site inhibitory ligands require the presence of an intact adenine ring. Inhibitory activity is enhanced in 2′-deoxy- (2′-d-) and especially 2′,5′-dideoxy (2′,5′-dd-) derivatives, and there is a strong preference for 3′-phosphates. P-site inhibitors are not competitive with activators such as Mn^{2+}, forskolin or $G_{5}\alpha$, and they are much more potent inhibitors of activated than of basal enzyme activity.

A number of adenine nucleoside 3′-polyphosphates have been synthesized. The successive addition of phosphate groups to the 3′-position increases inhibitory potency. The most potent compounds were 2′-d-3′-ADP (IC_{50} ~140 nM), 2′-d-3′-ATP (IC_{50} ~90 nM), 2′,5′-dd-3′-ADP (IC_{50} ~100 nM), 2′,5′-dd-3′-ATP (IC_{50} ~40 nM), and 2′,5′-dd-3′-A4P (IC_{50} ~7 nM).[4] These compounds are noncompetitive inhibitors of type I AC from bovine brain, consistent with inhibition via the P-site. 2′5′-dd-3′-ADP is a precursor to 2′,5′-dd-3′-ATP. Since 3′-ADP and 3′-ATP are naturally occurring, this class of compounds may regulate adenylyl cyclases *in vivo*.

Preparation Instructions

2′,5′-dd-3′ ADP is soluble in water at >10 mg/ml.

Storage/Stability

Store tightly sealed at –20 °C, desiccated.

References

1. Tesmer, J.J.G., et al., Molecular basis for P-site inhibition of Adenylyl cyclase. Biochemistry, **39,** 14464-14471 (2000).
2. Desaubry, L. and Johnson, R.A., Adenine nucleoside 3'-tetraphosphates are novel and potent inhibitors of adenylyl cyclases. J. Biol. Chem., **273**, 24972-24977 (1998).
3. Dessauer, C.W., et al., The interactions of adenylate cyclases with P-site inhibitors. Trends Pharmacol. Sci., **20**, 205-210 (1999).
4. Johnson, R.A., et al., Isozyme-dependent sensitivity of adenylyl cyclases to P-site-mediated inhibition by adenine nucleosides and nucleoside-3'-polyphosphates. J. Biol. Chem., **272**, 8962-8966 (1997).

AH 9/01