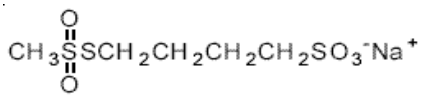
FT-AM366A

MTSBS

Reacts specifically and rapidly with thiols to form mixed disulfides. Used for study of protein topology and ion channels.

Product Description

Name :	**MTSBS** 4-sulfonatobutyl methanethiosulfonate sodium salt
Catalog Number :	FP-AM366A, 250 mg
Structure :	CAS [385398-78-7] $C_5H_{11}NaO_5S_3$
Molecular Weight :	MW= 520,49
Solubility:	DMSO, DMF, MeOH, Water
Absorption / Emission :	$\lambda_{exc}\backslash\lambda_{em}$ (MeOH) = 556/575nm $\lambda_{exc}\backslash\lambda_{em}$ (water) = 520/595nm
EC (M^{-1} cm^{-1}) **:**	

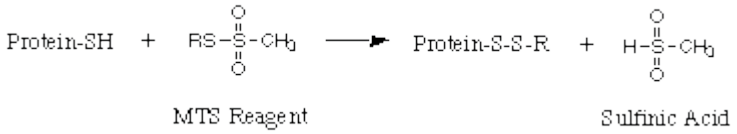


Storage: -20°C Protect from light and moisture. Highly hydroscopic !

Introduction

The combination of site-specific mutagenesis, and the use of MTS reagents is a powerful technique for probing the structures and function of proteins.

The science of the mapping of membrane proteins has advanced considerably with the advent of cloned and expressed membrane proteins and the use of site-directed mutagenesis. A useful strategy is to introduce individual cysteine residues at various positions in a membrane protein, and then test the surface accessibility of these cysteines using thiol-specific reagents. With ion-channels, the chemical modification of an introduced cysteine may produce a measurable change in the function of the channel,which can be monitored by electrophysiological recording, thereby affording information concerning the time-course, state dependence and membrane-sidedness of the accessibility of that cysteine (Akabas *et. al*. 1992). This approach applied to membrane-spanning segments of ion channels and transport proteins is called the substituted-cysteine-accessibility method (SCAM; Akabas *et al*., 1994)



Advantages of MTS Reagents

Sulfhydryl active reagents have had a long history of use as blocking and labeling groups, reporter groups, cross-linking groups and affinity labeling groups for the chemical modification of peptides and proteins (for a good review of the state of the art to 1977 see Kenyon and Bruice, 1977 and references therein). The traditional reagents include such reactive functionalities as maleimides, iodoacetates, and organomercurials. These are in general slow to react, therefore require long reaction times, and large excess of reagent. The recently developed alkylthiosulfonates are distinguished by their extremely rapid reactivity under the mild conditions necessary for successful electrophysiological recording experiments, their high selectivity for cysteinyl sulfhydryls, their ability to effect quantitative and complete conversion to the disulfide without applying a large excess of reagent, the general reversibility of the formation of disulfide bond upon the addition of thiols such a ß-mercaptoethanol

or dithiothreitol (Kenyon and Bruice, 1977 and references therein), and the wide range of functionality accommodated in the R group. The treatment of several larger proteins containing the full complement of the standard amino acids with Methyl methanethiosulfonate (MMTS) resulted in selective reaction of only cysteinyl sulfhydryls (Smith et. al. 1975; Kenyon and Bruice, 1977). This selectivity is due in part to the fact that at physiological pH values, amino groups are essentially completely protonated (Bruice and Kenyon, 1982). Even at mM concentration of proteins, stoichiometric sulfhydryl group modification may be achieved in solutions of either anhydrous organic or buffered aqueous and aqueous-organic solvents. Also, the sulfinic acid byproduct of the reaction of a sulfhydryl with a methanethiosulfonate, decomposes rapidly to low-molecular-weight volatile products which do not, in general, affect the stability of the disulfide bond formed, or the activity of the enzyme (see Bruice and Kenyon, 1982 and references therein).

Directions for use

Guidelines for use

Arthur Karlin and his colleagues introduced three charged MTS reagents, 2-Aminoethyl methanethiosulfonate hydrobromide (MTSEA), Sodium (2-sulfonatoethyl) methanethiosulfonate (MTSES), and [2-(Trimethylammonium)ethyl] methanethiosulfonate bromide (MTSET). These reagents were used in conjunction with site specific introduction of cysteines to study the structure and function of ion channel proteins (SCAM). Because these reagents introduce a positive or negative charge at the position of a previously neutral cysteine residue they frequently give a functional change in a channel protein that can be measured by electrical recording (Stauffer, 1994a; Akabas, 1992).

SCAM and the charged MTS reagents have been successfully applied to the structural and functional elucidation of a number of ligand-gated ion channels, including muscle acetylcholine receptor (Akabas, 1992, 1994a, 1995), neuronal acetylcholine receptor (Ramirez-Latorre, 1996), GABA receptor (Xu, 1993, 1996), NMDA glutamate receptor (Kuner, 1996), and cyclic nucleotide gated channels (Sun, 1996). This technique has also been applied to the cystic fibrosis transmembrane conductance regulator (Akabas, 1994b), and to voltage-gated potassium (Pascual et al., 1995; Kürz et al., 1995) and sodium channels (Yang 1996). SCAM has also been used to map the ligand-binding domain of the seven-transmembrane-helices, G-protein-linked dopamine receptor (Javitch, 1995; Fu., 1996).

The serotonin transporter belongs to a large family of integral membrane proteins responsible for terminating the action of neurotransmitters released from presynaptic neurons. Gary Rudnick and his colleagues used site-directed mutagenesis and MTS reagents to study this transporter (Humphreys, 1994; J.-G. Chen., 1997) and have identified the specific amino acid residues important for binding serotonin and cocaine and for conformational changes (G. Rudnick, private communication).

Ion channels are dynamic transmembrane proteins that undergo conformational changes when they open and close. Several physiologically important factors influence this gating process, including binding of agonists and changes of the transmembrane potential. However the way the channel protein transduces these signals into gating is largely unknown. Dick Horn and his colleagues have studied a particular voltage-dependent conformational change in sodium channels, which are responsible for the action potential in excitable cells. Using site-specific mutagenesis, they showed that the transmembrane potential affects the accessibility of the cysteine residues to the methanethiosulfonate reagents MTSES and MTSET (Yang, 1995; 1996).

Protocol may be found in the literature.

References

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- **Javitch, J.** *et al*. Mapping the binding site crevice of the dopamine D2 receptor by the substituted-cysteine accessibility method. *Neuron* 14: 825-831 (1995)
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- **Yang, N**., *et al*. Molecular basis of charge movement in voltage-gated sodium channels. *Neuron* 16: 113-122 (1996)

Technical and scientific information

Related / associated products and documents

See BioSciences Innovations catalogue and e-search tool.

- MTSES, FP-AM372A
- Paraformaldehyde 4% solution, DX9870
- D-Sorbitol, 303562

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