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PROPANETHIAL S-OXIDE: THE CULPRIT FOR LACHRYMATION DURING ONION/GARLIC CHOPPING

PROF. DR. DHRUBO JYOTI SEN

Department of Pharmaceutical Chemistry, Shri Sarvajanik Pharmacy College, Gujarat Technological University, Arvind Baug, Mehsana-384001, Gujarat, India

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Abstract: It is well known that people 'cry' when chopping onion/garlic but why is this so? The answer is that propanethial S-oxide (often referred to as thiopropanal S-oxide) is released into the air during chopping. Propanethial S-oxide is a lachrymator, an irritant that causes the eyes to fill with tears without damaging them. When a lachrymator comes into contact with the surface of the eye, the cornea, it is detected by the nervous system and triggers a response from the lachrymal (tear) glands. Tears are then produced in order to dilute the irritant. Propanethial S-oxide is relatively volatile and when its vapours come into contact with the eye a small amount reacts to form sulfuric acid, causing the burning and itching sensations that accompany the tears.

Interestingly, onion/garlic do not contain propanethial S-oxide and it is thought that onion/garlic produce this tear inducing compound to protect the plant from herbivores. It is the product of a series of chemical reactions that occur once the onion/garlic has been damaged. Onion/garlic have many sulfur containing molecules within them, but the precursor to propanethial S-oxide has been identified as the amino acid S-1-propenyl-L-cysteine sulfoxide (which is very similar to the chemical alliin, found in garlic). Cells are broken open as the onion/garlic cut and this releases the enzyme alliinase and water, which react with S-1-propenyl-L-cysteine sulfoxide forming a mixture of products. These products are the precursors for a variety of compounds that form the flavour of onion/garlic and include 1-propenyl sulfenic acid. The lachrymator propanethial S-oxide is formed from 1-propenyl sulfenic acid in an enzyme catalyzed reaction. It was originally thought that alliinase was responsible for this reaction. However, five years ago scientists in Japan identified another enzyme present in onion/garlic that carried out this process and named it lachrymatory-factor synthase.

Keywords: *Syn*-propanethial S-oxide, Sulfenic acid, LFS, Alliin, Allicin, Allinase

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Corresponding Author: PROF. DR. DHRUBO JYOTI SEN

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INTRODUCTION

Freshly cut onion (*Allium cepa*)/garlic (*Allium sativum*) often cause a stinging sensation in the eyes of people nearby, and often uncontrollable tears. This is caused by the release of a volatile gas, *syn*-propanethial-S-oxide, which stimulates nerves in the eye creating a stinging sensation. This gas is produced by a chain of reactions which serve as a defense mechanism: chopping an onion/garlic causes damage to cells which releases enzymes called alliinases. These break down amino acid sulfoxides and generate sulfenic acids. A specific sulfenic acid, 1-propenesulfenic acid, is rapidly acted on by a second enzyme, the lachrymatory factor synthase, producing the *syn*-propanethial-S-oxide. This gas diffuses through the air and soon reaches the eyes, where it activates sensory neurons. Lachrymal glands produce tears to dilute and flush out the irritant.[1]

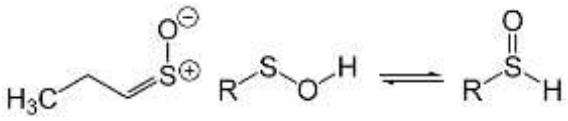

Figure-1: *syn*-propanethial-S-oxide and sulfenic acids

***syn*-Propanethial *S*-oxide** (C_3H_6OS), a member of a class of organosulfur compounds known as thiocarbonyl *S*-oxides (formerly "sulfines"), is a liquid that acts as a lachrymatory agent (triggers tearing and stinging on contact with the eyes). The chemical is released from onion/garlic, *Allium cepa*, as they are sliced. The release is due to the breaking open of the onion/garlic cells and their releasing enzymes called alliinases, which then break down amino acid sulfoxides, generating sulfenic acids.[2]

A **sulfoxide** is a chemical compound containing a sulfinyl (SO) functional group attached to two carbon atoms. It is a polar functional group. Sulfoxides are the oxidized derivatives of sulfides. Examples of important sulfoxides are alliin, a precursor to the compound that gives freshly crushed garlic its aroma and DMSO, a common solvent. A specific sulfenic acid, 1-propenesulfenic acid, formed when onion/garlic are cut, is rapidly rearranged by a second enzyme, called the lachrymatory factor synthase or LFS, giving *syn*-propanethial *S*-oxide. The gas diffuses through the air and on contact with the eye, it stimulates sensory neurons creating a stinging, painful sensation. Tears are released from the tear glands to dilute and flush out the irritant. Recently, a structurally related lachrymatory compound, *syn*-butanethial *S*-oxide, C_4H_8OS, has been found in another genus *Allium* plant, *Allium siculum*. Eye irritation can be avoided by cutting onion/garlics under running water or submerged in a basin of water.[3] Leaving the root end intact also reduces irritation as the onion/garlic base has a higher concentration of sulphur compounds than the rest of the bulb. Refrigerating the onion/garlic before use reduces the enzyme reaction rate and using a fan can blow the gas away from the

eyes. The more often one chops onion/garlic, the less one experiences eye irritation. A **sulfenic acid** is an organosulfur compound and oxoacid with the general formula RSOH. It is the first member of the family of organosulfur oxoacids, which also include sulfinic acids and sulfonic acids, RSO_2H and RSO_3H, respectively. The base member of the sulfenic acid series with R=H is hydrogen thioperoxide.[4]

Figure-2: Chopped onion/garlic and tears

In contrast to sulfinic and sulfonic acids, simple sulfenic acids, such as methanesulfenic acid, CH_3SOH, are highly reactive and cannot be isolated in solution. In the gas phase the lifetime of methanesulfenic acid is about one minute. The gas phase structure of methanesulfenic acid was found by microwave spectroscopy (rotational spectroscopy) to be $CH_3–S–O–H$. Sulfenic acids can be stabilized through steric effects, which prevent the sulfenic acid from condensing with itself to form thiosulfinates, RS(O)SR, such as allicin from garlic. Through the use of X-ray crystallography, the structure of such stabilized sulfenic acids were shown to be R–S–O–H. The stable, sterically hindered sulfenic acid, 1-triptycenesulfenic acid, has been found to have a pKa of 12.5 and an O–H Bond-Dissociation Energy (BDE) of 71.9±0.3kcal/mol, which can be compared to a pKa of ≥14 and O–H BDE of ~88 kcal/mol for the (valence) isoelectronic hydroperoxides, ROOH.[5]

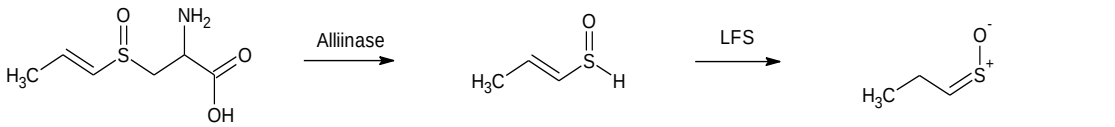

Figure-3: Mechanism

2-amino-3-[(1*E*)-prop-1-en-1-ylsulfinyl]propanoic acid is *S*-1-propenyl-*L*-cysteine sulfoxide (alliin) which reacts with alliinase to form (1*E*)-1-(oxido-λ^4-sulfanyl)prop-1-ene (sulfenic acid) and that reacts with lachrymatory factor synthase (LFS) to produce *syn*-Propanethial S-oxide.

Sulfenic acids are produced by the enzymatic decomposition of alliin and related compounds following tissue damage to garlic, onion/garlic and other plants of the Allium genus. 1-

Propenesulfenic acid, formed when onion/garlic is cut, is rapidly rearranged by a second enzyme, the lachrymatory factor synthase, giving *syn*-propanethial-S-oxide. 2-Propenesulfenic acid, formed from allicin, is thought to be responsible for garlic's potent antioxidant activity. Mass spectrometries with a DART ion source were used to identify 2-propenesulfenic formed when garlic is cut or crushed and to demonstrate that this sulfenic acid has a lifetime of less than one second.[6] The pharmacological activity of certain drugs, such as omeprazole, esomeprazole, ticlopidine, clopidogrel and prasugrel is proposed to involve sulfenic acid intermediates. Oxidation of cysteine residues in protein to the corresponding protein sulfenic acids is suggested to be important in redox-mediated signal transduction. Alliin is a sulfoxide that is a natural constituent of fresh garlic. It is a derivative of the amino acid cysteine. When fresh garlic is chopped or crushed, the enzyme alliinase converts alliin into allicin, which is responsible for the aroma of fresh garlic.[7]

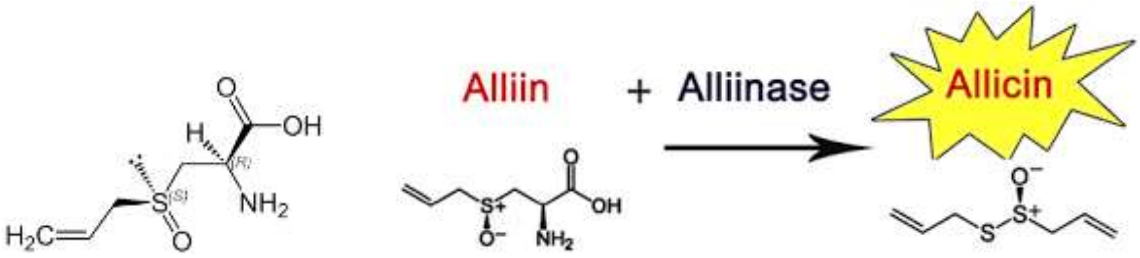

Figure-4: Alliin (2R)-2-amino-3-[(S)-prop-2-enylsulfinyl]propanoic acid)

Garlic has been used since antiquity as a therapeutic remedy for certain conditions now associated with oxygen toxicity and when this was investigated, garlic did indeed show strong antioxidant and hydroxyl radical-scavenging properties, it is presumed owing to the alliin contained within. Alliin has been found to affect immune responses in blood. Alliin was the first natural product found to have both carbon- and sulfur-centered stereochemistry. Sulfenate-based ligands are found at the active site of the nitrile hydratases. The S-O group is proposed as the nucleophile that attacks the nitrile.[8]

Conclusion

Onion/garlic produces the chemical irritant known as *syn*-propanethial-S-oxide. It stimulates the eyes' lachrymal glands so they release tears. Scientists used to blame the enzyme allinase for the instability of substances in a cut onion/garlic. Recent studies from Japan, however, proved that lachrymatory-factor synthase, (a previously undiscovered enzyme) is the culprit.

The process goes as follows:

1. Lachrymatory-factor synthase is released into the air when we cut an onion/garlic.

2. The synthase enzyme converts the amino acids sulfoxides of the onion/garlic into sulfenic acid.
3. The unstable sulfenic acid rearranges itself into syn-propanethial-S-oxide.
4. Syn-propanethial-S-oxide gets into the air and comes in contact with our eyes. The lachrymal glands become irritated and produce the tears!

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