

Synthesis and pharmacological activity of small organosulfur molecules for natural products mimicking

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Abstract

Garlic belongs to the *Allium* genus plants. It has a bewildering number of molecules, and organosulfur compounds are the most representatives. The most known and studied molecule and the most abundant is alliin. This molecule is produced from alliin, by the action of the enzyme alliinase that together are released after crashing the garlic bulb. Alliin has many pharmacological activities and there are many papers available in literature about the studies of its properties. One of the main problems of this molecules is the considerable instability. Diallyl disulfide is the most important decomposition product of alliin. Many studies were carried out in the past years about this molecule, regarding biological activity and stability. We recently developed a green procedure to obtain saturated and unsaturated thioacetates starting from organic methanesulfonates.

This procedure use water as solvent and avoid the use of a catalyst. Thioacetates are easily hydrolyzed to thiols and thiols are easily converted to symmetrical disulfides by an oxidation reaction. One of the most important properties of diallyl disulfide is the anticancer activity. Some researchers have recently proved in vitro, the antitumoral activity of this molecule against lung cancer cells with apoptosis and cell cycle arrest. There are many studies that prove that the allylic double bonds play an important role. We synthesized different symmetric disulfides for mimicking this molecule, with double bonds in different positions and with different substituents. We have obtained interesting result in vitro, using A549 lung cancer cells line, that prove that allylic double bond is not the most important driving force, but other factors like substituents or the position of the unsaturation site can affect the activity. We have two new substrates that are quite similar but show higher activity than diallyl disulfide that can open new synthetic routes and studies in this direction.

Sulfur contributes significantly to nature chemical diversity and thanks to its features allows fundamental biological reactions that no other element allows. Sulfur natural compounds are utilized by all living beings and depending on the function are distributed in the different kingdoms. It is no coincidence that marine organisms are one of the most important sources of sulfur natural products since most of the inorganic sulfur is

metabolized in ocean environments where this element is abundant. Terrestrial organisms such as plants and microorganisms are also able to incorporate sulfur in organic molecules to produce primary metabolites (e.g., methionine, cysteine) and more complex unique chemical structures with diverse biological roles. Animals are not able to fix inorganic sulfur into biomolecules and are completely dependent on preformed organic sulfur compounds to satisfy their sulfur needs. However, some higher species such as humans can build new sulfur-containing chemical entities starting especially from plants' organosulfur precursors. Sulfur metabolism in humans is very complicated and plays a central role in redox biochemistry. The chemical properties, the large number of oxidation states, and the versatile reactivity of the oxygen family chalcogens make sulfur ideal for redox biological reactions and electron transfer processes. This review will explore sulfur metabolism related to redox biochemistry and will describe the various classes of sulfur-containing compounds spread all over the natural kingdoms. We will describe the chemistry and the biochemistry of well-known metabolites and of the unknown and poorly studied sulfur natural products which are still in search for a biological role.

Natural products (NPs) have a long history as a source of, and inspiration for, novel agrochemicals. Many of the existing herbicides, fungicides and insecticides have their origins in a wide range of NPs from a variety of sources. Due to the changing needs of agriculture, shifts in pest spectrum, development of resistance and evolving regulatory requirements, the need for new agrochemical tools remains as critical as ever. As such, NPs continue to be an important source of models and templates for the development of new agrochemicals, demonstrated by the fact that NP models exist for many of the pest control agents that were discovered by other means. Interestingly, there appear to be distinct differences in the success of different NP sources for different pesticide uses. While a few microbial NPs have been important starting points in recent discoveries of some insecticidal agrochemicals, historically plant sources have contributed the most to the discovery of new insecticides. In contrast, fungi have been the most important NP sources for

new fungicides. Like insecticides, plant sourced NPs have made the largest contribution to herbicide discovery. Available data on 2014 global sales and numbers of compounds in each class of pesticides indicate that the overall impact of NPs to the discovery of herbicides has been relatively modest compared to impact observed for fungicides and insecticides. However, as new sourcing and approaches to NP discovery evolve, the impact of NPs in all agrochemical arenas will continue to expand.

Organosulfur compound, also spelled organosulphur compound, also called organic sulfur compound, a subclass of organic substances that contain sulfur and that are known for their varied occurrence and unusual properties. They are found in diverse locations, including in interstellar space, inside hot acidic volcanoes, and deep within the oceans. Organosulfur compounds occur in the bodies of all living creatures in the form of certain essential amino acids (such as cysteine, cystine, and methionine, which are components of proteins), of the tripeptide glutathione, and of enzymes, coenzymes, vitamins, and hormones.