

Chemistry in a salad bowl: Comparative organosulfur chemistry of garlic, onion and shiitake mushrooms

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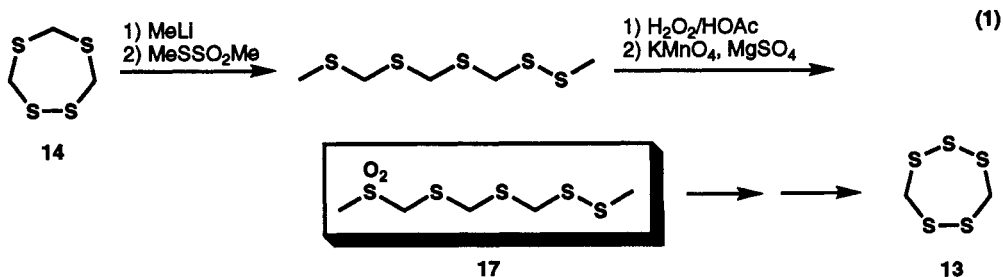
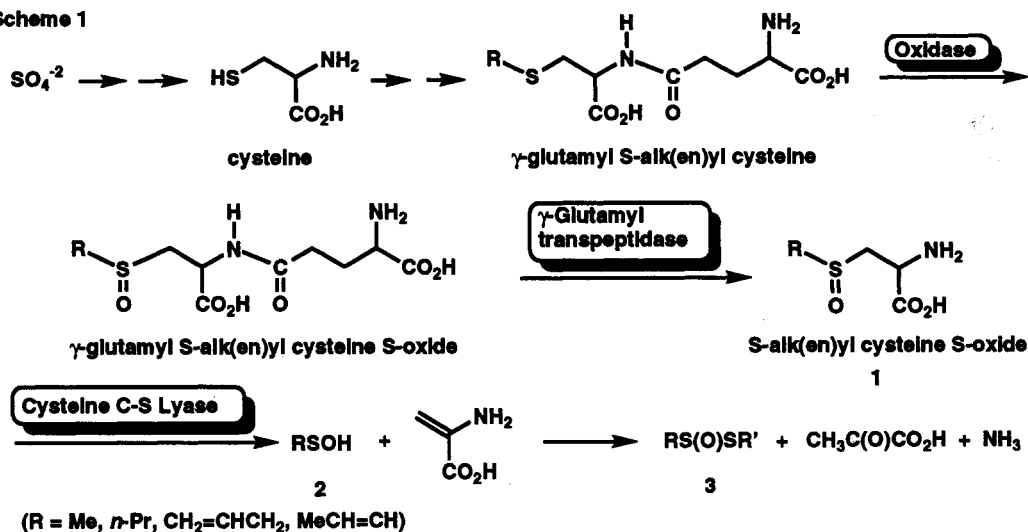
Abstract: - Enzymatic processes similar to those which release the organosulfur flavorants in *Allium* spp. (garlic, onion) are also seen in shiitake mushroom (*Lentinus edodes*). By comparing the chemistry following the final enzymatic cleavage step in these plants, the structure proposed for the precursor "SE-3" of the shiitake mushroom flavorant lenthionine is found to be incorrect. An alternative structure for SE-3, 2,3,5,7,9-pentathiadecane 9,9-dioxide, is proven by a brief total synthesis.

It has long been known that the characteristic flavors of garlic (*Allium sativum*), onion (*A. cepa*) and other genus *Allium* plants, detected when these plants are cut or crushed, are produced by the action of C-S lyase enzyme (alliinases) on S-alkyl cysteine S-oxide precursors of type $RS(O)CH_2CH(NH_2)COOH$ (1), where R is variously Me, *n*-Pr, allyl, or 1-propenyl. The initially released sulfenic acid RSO_2H , 2, can then condense with itself or other sulfenic acids to form thiosulfinate esters, $RS(O)SR'$ (3) and, when R = 1-propenyl, rearrange to the onion lachrymatory factor propanethial S-oxide, $EtCH=S=O$ (4). As we have shown, a variety of other unusual cyclic and acyclic organosulfur compounds can result from subsequent or parallel reactions involving 2-4. Compounds of type 1 are thought to originate from cysteine through a series of steps culminating in oxidation of γ -glutamyl-S-alk(en)yl cysteines by oxidases to the corresponding S-oxides followed by cleavage of these to 1 by γ -glutamyl transpeptidases (Scheme 1)(1).

The types of reactions summarized in Scheme 1 are not limited to genus *Allium* plants. Thus, similar reactions are seen in *Brassica* vegetables such as broccoli, Brussels sprouts, cabbage, and cauliflower, all of which contain $MeS(O)CH_2CH(NH_2)COOH$ and give $MeS(O)SMe$ on enzymatic cleavage (2). Particularly interesting examples of flavor generation by "Allium-like" pathways in very different species is illustrated by the mushrooms *Marasmius alliaceus* and *Lentinus edodes* (shiitake mushroom). The flavor precursor in the former mushroom, which, as suggested by its Latin name, develops "a strong, garlic like odor -- especially when wet or when crushed with water" (3), is γ -glutamyl marasmin, $MeSCHS(O)CH_2CH(CO_2H)NHC(O)CH_2CH_2CH(CO_2H)NH_2$ (5)(3). It is suggested that 5 is sequentially cleaved by a γ -glutamyl transpeptidase and by a C-S lyase giving $MeSCHS(O)CH_2CH(CO_2H)NH_2$ (6) followed by $MeSCH_2SOH$ (7). The latter is thought to disproportionate giving $(MeSCH_2S)_2$ (8), thought to be the actual odorous compound (3). Compounds related to 8 are formed as flavorants in a variety of species (4), suggesting that "dithio" flavor precursors of type 5 are widely distributed. For example the occurrence of $(MeSO_2CH_2S)_2$ in *Lentinus edodes* (5) suggests that $MeSO_2CHS(O)CH_2CH(CO_2H)NH_2$ (9) is the immediate precursor in the intact plant. Of particular interest is the occurrence in *Lentinus edodes* of lenticic acid, $MeSO_2CHS(O)CHS(O)CHS(O)CH_2CH(CO_2H)NHC(O)CH_2CH_2CH(CO_2H)NH_2$ (10) (6), a "tetrathio" flavor precursor with a structure curiously reminiscent of that of the polyketides. Sequential cleavage of 10 by a γ -glutamyl transpeptidase followed by a C-S lyase should give $MeSO_2CHS(O)CHS(O)CHS(O)CH_2CH(CO_2H)NH_2$ (11) followed by $MeSO_2CHS(O)CHS(O)CHSOH$ (12). The subsequent chemistry, which is not well understood, ultimately results in the formation of lenthionine (13) and related polythio heterocycles such as 14 (7). The fate of the oxygen atoms other than that on the cysteine sulfur is unclear, since lenthionine and the other cyclic products lack oxygen. Precursors such as $MeSO_nCHSCHSCHSCH_2CH(CO_2H)NH_2$ (15) may also be involved, although these have not yet been reported.

Compounds 13 and 14 are claimed to be formed from precursor SE-3, a colorless solid of mp 80–82 °C, identified as 2,3,7,9-tetrathia-5-oxadecane 2,2,9-trioxide (16)(7), $MeSO_2SCH_2OCH_2SCH_2S(O)Me$ which in turn is presumably formed from 12. Because there is no obvious mechanism connecting intermediate 12 with 16, we reexamined the structure proof for this latter compound.

Scheme 1



While the $\text{C}_5\text{H}_{12}\text{S}_4\text{O}_4$ formula of **16** is consistent with the low resolution mass spectral m/e 264 parent ion, the reported ^1H NMR spectrum (δ 2.50 (3 H, s), 3.05 (3 H, s), 3.97 (2 H, s), 4.05 (2 H, s), and 4.19 (2 H, s) ppm) is incompatible with structure **16** since the α -, γ -, and ϵ -sulfinyl CH_2 protons should be diastereotopic, and since the chemical shift of 4.05 and 4.19 ppm for the OCH_2S groups is at too high a field compared to chemical shifts for this position in 1,3-thioxane and related compounds (ca. 4.7-5.0 ppm)(8). In addition, the infrared bands at 977, 962 and 953 cm^{-1} "ascribable to a sulfoxide" are in fact far outside the known range of 1040-1065 cm^{-1} . Finally, many of the electron-impact mass spectral fragmentation processes proposed for **16** seem improbable. We suggest an alternative structure for SE-3, namely 2,3,5,7,9-pentathiadecane 9,9-dioxide (**17**), $\text{MeSO}_2\text{CH}_2\text{SCH}_2\text{SCH}_2\text{SSMe}$ and have proven this suggestion by a brief total synthesis (eq 1)(9). Compound **17**, a colorless solid of mp 79-80.5 $^\circ\text{C}$ with spectroscopic properties identical to those reported for **16**, could originate from condensation reactions involving sulfenic acids $\text{MeSO}_2\text{CH}_2\text{SCH}_2\text{SCH}_2\text{SOH}$ and MeSOH .

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