

SUPPLEMENTARY INFORMATION

Mechanistic studies on the reactivity of sensitizing allylic hydroperoxides: investigation on the covalent modification of amino acids by carbon-radical intermediates

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Reaction **4**/*N*-Ac-Cys-OMe

ESI-MS/MS analysis of *m/z* 346 and *m/z* 364

Reaction **3**/*N*-Ac-Lys-OMe/FeSO₄

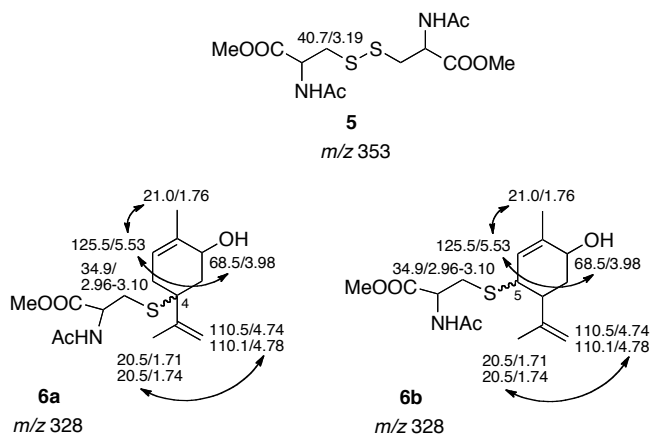
LC chromatogram of the crude product

Reaction **3**/*N*-Ac-Tyr-OEt/FeCl₃

LC chromatogram of the reaction and suggested adduct **30**

NMR data compounds 5, 6a/6b

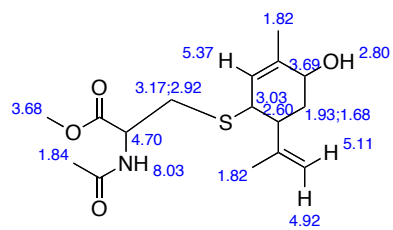
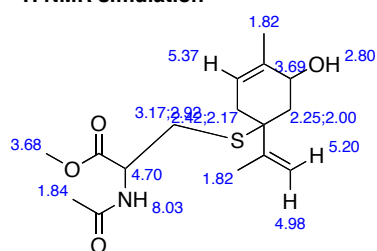
In the presence of FeCl₃, two fractions of new compounds could be isolated from the crude product by column chromatography on silica gel (acetone/pentane 1:9, acetone/pentane 2:8) and analyzed by NMR. One corresponded to the cysteine disulfide dimer **5**, resulting from its oxidation. HSQC experiments showed two protons at 3.19 ppm correlated to a carbon atom at 40.7 ppm, δ characteristic of the -CH₂ in position α to the disulfide bond. NMR analysis of the second fraction suggested the formation of two diastereomers. HSQC data revealed carbon atoms at 110.5/110.1 ppm, directly correlated to protons at 4.74/4.78 ppm, proving that the vinyl group of **3** had been preserved during the reaction. HMBC experiments showed long-range correlations between protons at 4.74/4.78 ppm and a carbon atom at 20.5 ppm bearing protons at 1.71/1.74 ppm, corroborating the existence of the isoprenyl group. HSQC and HMBC data also highlighted a correlation between a carbon atom at 125.5 ppm and a proton at 5.53 ppm, this one long-range correlated with a methyl group at 21.0/1.76 ppm and a carbon atom at 68.5 ppm with an associated proton at 3.98 ppm. These δ suggested the replacement of the initial hydroperoxide methylallyl group of **3** by a secondary alcohol methylallyl function, confirming the preservation of the menthene ring. Finally, both diastereomers had a *N*-Ac-Cys-OMe unit linked as the characteristic δ of the -CH₂ in position α to the thiol group of the side-chain at 27.2 ppm shifted to 34.9 ppm with protons at 2.96/3.10 ppm. The whole NMR information agreed with regioisomers **6a** and **6b**, for which two diastereomers are possible.



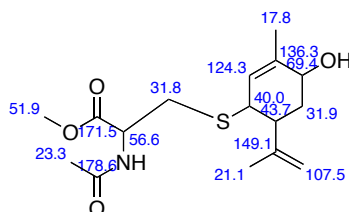
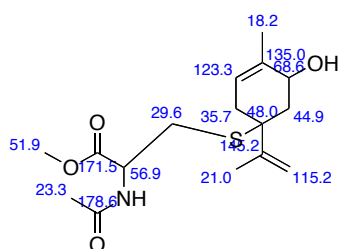
Combination of NMR (HSQC direct and HMBC long-range correlations) and MS data suggesting structures **5** and **6a/6b**.

NMR data did not allow distinguishing between regioisomers **6a** and **6b**. Theoretically, ¹H and ¹³C NMR chemical shifts of the isoprenyl group and of the sulphur atom fixing position should be slightly different. However, no significant signal was observed discriminating between both derivatives.

¹H NMR simulation



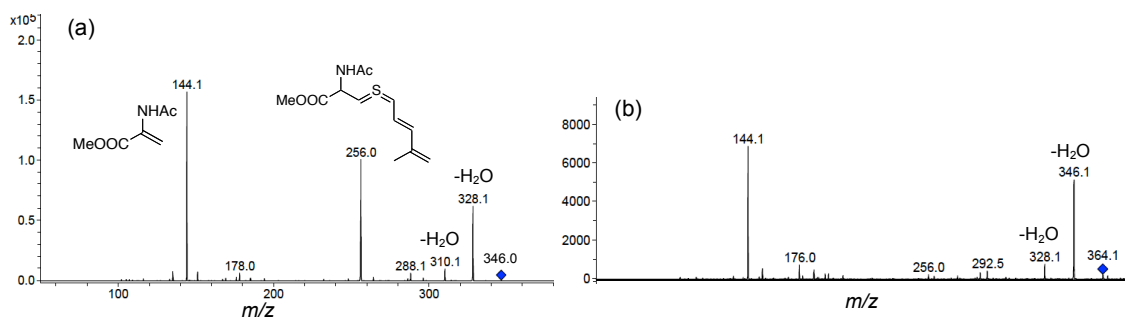
¹³C NMR simulation



Simulation of NMR chemical shifts of **6a** and **6b** (CS Chem Draw Ultra software, version 12.0)

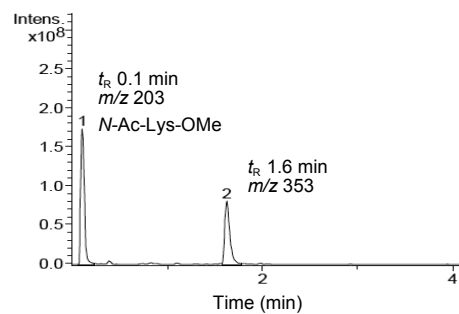
Reaction 4/*N*-Ac-Cys-OMe

(a) ESI-MS/MS analysis of *m/z* 346; (b) ESI-MS/MS analysis of *m/z* 364



Reaction 3/*N*-Ac-Lys-OMe/ FeSO_4

LC chromatogram of the crude product



Reaction 3/*N*-Ac-Tyr-OEt/ FeCl_3

LC chromatogram of the reaction and suggested adduct **30**

