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Supporting Information

Antioxidant Generation and Regeneration in Lipid Bilayers: the Amazing Case of Lipophilic Thiosulfinates and Hydrophilic Thiols

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Experimental Procedures

Liposome preparation. Egg phosphatidylcholine (Egg PC) was weighed (75 mg) in a dry vial and dissolved in a minimum volume of chloroform. The solvent was then evaporated under argon to yield a thin film on the vial wall. The film was left under vacuum for 2 hours to remove any remaining solvent. The lipid film was then hydrated with 4.0 mL of a 10 mM phosphate buffered-saline (PBS) solution (pH 7.4) containing 150 mM NaCl, yielding a 24 mM lipid suspension. The lipid suspension was then subjected to 10 freeze-thaw-sonication cycles, where each cycle involved storing the vial with the solution in dry ice for 4 minutes, thawing at room temperature for 4 minutes, followed by 4 minutes of sonication. The lipid suspension was then extruded 30 times using a mini-extruder equipped with a 100 nm polycarbonate membrane.

Inhibited oxidations. To individual 36 μL aliquots of the 24 mM liposome solution were added increasing amounts (2, 4, 6, 8, 10 and 20 μL, respectively) of a solution of the test antioxidant in acetonitrile (640 μM) and 10 μL of a solution of H_2B-PMHC in acetonitrile (13 μM). Each resultant solution was then diluted to 800 μL with PBS, from which 280 μL of each was loaded into a well of a 96-well microplate. The solution was equilibrated to 37°C for 5 min, after which 20 μL of a solution of azo compound (41 mM in 2,2'-azobis-(2-amidinopropane)monohydrochloride (ABAP) in PBS or 3 mM in 2,2'-azobis-(4-methoxy-2,4-dimethylvaleronitrile) (MeOAMVN) in acetonitrile) was added to each well using the reagent dispenser of a microplate reader. The fluorescence was then monitored for 6 h at 50 s time intervals (λ_{ex} = 485 nm; λ_{em} = 520 nm). The final solutions in each well were 1 mM in lipids, 0.15 μM in H_2B-PMHC, 2.7 mM in ABAP or 0.2 mM in MeOAMVN and either 1.5, 3.0, 4.5, 6.0, 7.5 or 15 μM in antioxidant. Each liposome contained, on average, 15 fluorophores with an EggPC/fluorophore molar ratio of 6700:1. Under these conditions, no fluorescence self-quenching was expected to occur within the liposome bilayer.[1]

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Co-inhibited oxidations with antioxidant and an equivalent amount of NAC. To individual 36 μL aliquots of the 24 mM liposome solution were added increasing amounts (27, 45 and 90 μL) of solutions of *N*-acetylcysteine (NAC) in PBS (143 μM). To each sample was then added increasing amounts (6, 10, 20 μL, respectively) of a solution of the test antioxidant in acetonitrile (643 μM) or simply 6 μL of acetonitrile, followed by 10 μL of a solution of H_2B-PMHC in acetonitrile (13 μM). Each resultant solution was then diluted to 800 μL with PBS, from which 280 μL was loaded into a well of a 96-well microplate. The microplate was equilibrated to 37°C for 5 min, after which 20 μL of a solution of MeO-AMVN in acetonitrile (3 mM) or ABAP (41 mM) was added to each well using the reagent dispenser of a microplate reader. The fluorescence was then monitored for 6 h at 50 s time intervals (λ_{ex} = 485 nm; λ_{em} = 520 nm). The final solutions in each well were 1 mM in lipids, 0.15 μM in H_2B-PMHC, 0.2 mM in MeOAMVN or 2.7 mM in ABAP, 4.5, 7.5 or 15 μM in antioxidant, and 4.5, 7.5 or 15 μM in NAC.

Co-inhibited oxidations with the same amount of antioxidant and increasing amount of NAC. To individual 36 μL aliquots of the 24 mM liposome solution were added increasing amounts (27, 54, 81 or 135 μL for **9**, 0, 27, 54, 108 μL for **5**, respectively) of solutions of *N*-acetylcysteine (NAC) in PBS (142.84 μM). To the aliquots of samples were then added 6 μL of a solution of the test antioxidant in acetonitrile (643 μM) , followed by 10 μL of a solution of H_2B-PMHC in acetonitrile (13 μM). Each resultant solution was then diluted to 800 μL with PBS, from which 280 μL was loaded into a well of a 96-well microplate. The microplate was equilibrated to 37°C for 5 min, after which 20 μL of a solution of MeO-AMVN in acetonitrile (3 mM) or ABAP (41 mM) was added to each well using the reagent dispenser of a microplate reader. The fluorescence was then monitored for 6 h at 50 s time intervals (λ_{ex} = 485 nm; λ_{em} = 520 nm). The final solutions in each well were 1 mM in lipids, 4.5 μM in antioxidant, 0.15 μM in H_2B-PMHC, 0.2 mM in MeOAMVN or 2.7 mM in ABAP, 4.5, 9, 13.5 or 22.5 μM in NAC in liposomes supplemented with **9**, and 0, 4.5, 9 or 18 μM in NAC in liposomes supplemented with **5**.

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Decomposition of allicin and petivericin (50 μM) in liposomes. To a solution of liposome (24 mM, 89 μL) was added 25 μL of a solution of allicin or petivericin in acetonitrile (4.3 mM), which was then diluted to 2140 μL with PBS. The final solutions were 1 mM in lipids, 50 μM in antioxidant. The mixture was vortexed for 15 seconds and then placed in a sand bath pre-heated to 37°C for two hours. Samples (200 μL each) were taken from the mixture in fifteen-minute intervals, they were extracted with Et_2O (200 μL) containing either 3,4-dimethoxylbenzyl alcohol (1 μM, internal standard for the analysis of allicin) or dodecanoic acid (0.75 μM, internal standard for the analysis of petivericin). The extraction was performed by vortexing the mixture of aqueous reaction solution and Et_2O in a 1 mL centrifuge tube. After sitting still for 5 mins, the upper organic layer was taken by a 1mL syringe, which was then injected into a new 1 mL centrifuge tube. Et_2O was then removed under a stream of N_2. The residue was placed under vacuum for 5 mins, and then dissolved in 80 μL acetonitrile. The resulting solution was analyzed by LC-MS using an Atlantis C18, column (5 μm, 4.6×150 mm). For allicin, the mobile phase was 30% water and 70% acetonitrile flowing at 0.6 mL min^{-1}, and for petivericin, the mobile phase was 18% water, 81% acetonitrile and 1% methanol, flowing at 0.6 mL min^{-1}. Allicin was quantified by its UV response (λ = 234 nm; R_t= 3.07 min; 3,4-dimethoxylbenzyl alcohol: R_t= 4.06 min), whereas, for petivericin, MS (SIR) was used ($[M+H]^+$ = 263, R_t= 4.29 mins; dodecanoic acid: $[M-H]^-$ = 199, R_t= 8.30 mins).

Decomposition of allicin and petivericin (50 μM) with MeOAMVN (0.2 mM) in liposomes containing 0.15 μM H2B-PMHC. To a solution of liposome (24 mM, 89 μL) was added 25 μL of a solution of allicin or petivericin in acetonitrile (4.3 mM), followed by 25 μL of a solution of H_2B-PMHC in acetonitrile (13 μM). The resultant solution was then diluted to 2000 μL with PBS, to which 143 μL of a solution of MeOAMVN in acetonitrile (3 mM) was added. The final solutions were 1 mM in lipids, 50 μM in antioxidant, 0.15 μM in H_2B-PMHC and 0.2 mM in

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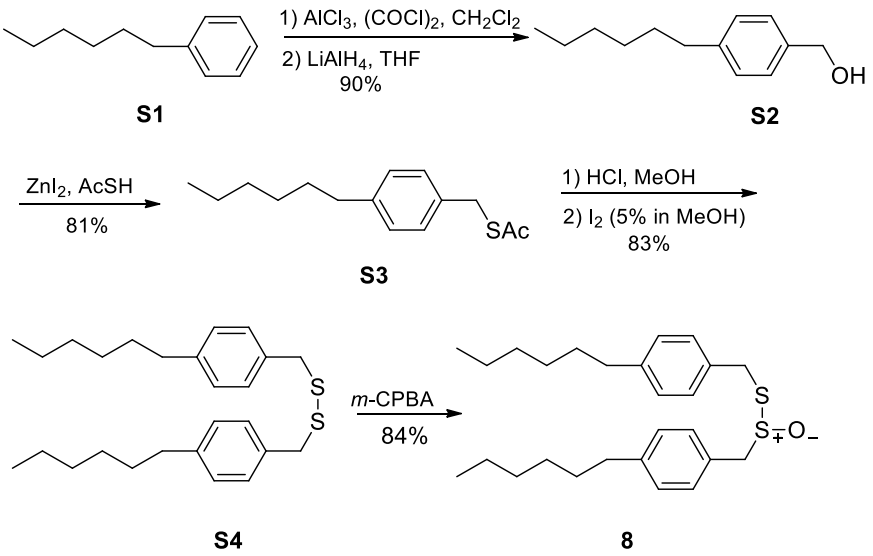
MeOAMVN. The mixture was vortexed for 15 seconds and then placed in a sand bath pre-heated to 37°C for two hours. Samples were taken, manipulated and analyzed as described above.

Decomposition of 2 and formation of mixed disulfide 11. To a solution of liposome (24 mM, 161 μL) was added 202 or 405 μL of a solution of NAC in PBS (143 μM), followed by 27 μL of a solution of petivericin in acetonitrile (1.07 mM) and 45 μL of a solution of H_2B-PMHC in acetonitrile (13 μM). The resultant solution was then diluted to 3600 μL with PBS, to which 257 μL of a solution of MeOAMVN in acetonitrile (3 mM) was added. The final solutions were 1 mM in lipids, 7.5 μM in **2**, 0.15 μM in H_2B-PMHC, 0.2 mM in MeOAMVN, and either 7.5 or 15 μM in NAC. The mixture was vortexed for 15 seconds and then placed in a sand bath pre-heated to 37°C for 30 mins. Samples (200 μL each) were taken from the mixture in one-minute intervals at the first ten minutes and then in five-minute intervals for another 20 minutes and extacted with acidic Et_2O (0.05% formic acid, 200 μL) containing dodecanoic acid (0.75 μM) as internal standard standard, which was further manipulated and analyzed as described above for the decomposition of 50 μM petivericin. For mixed disulfide **11**, MS (SIR) detection was used (disulfide **11**: $[M\text{-}H]^- = 284$, $R_t = 2.76$ mins).

Decomposition of 8 and formation of mixed disulfide 9. To a solution of liposome (24 mM, 89 μL) was added 113 or 225 μL of a solution of NAC in PBS (143 μM), followed by 15 μL of a solution of **9** in acetonitrile (1.07 mM) and 25 μL of a solution of H_2B-PMHC in acetonitrile (13 μM). The resultant solution was then diluted to 2000 μL with PBS, to which 143 μL of a solution fo MeOAMVN in acetonitrile (3 mM) was added. The final solutions were 1 mM in lipids, 7.5 μM in **8**, 0.15 μM in H_2B-PMHC, 0.2 mM in MeOAMVN, and either 7.5 or 15 μM in NAC. The mixture was vortexed for 15 seconds and then placed in sand bath pre-heated to 37°C for two hours. Samples (200 μL each) were taken from the mixture in fifteen-minute intervals and extacted with acidic Et_2O (0.05% formic acid, 200 μL) containing dodecanoic acid (0.75 μM) and *N*-phenylacetamide (0.1 μM) as internal standards. The samples were further

manipulated as described above and analyzed by LC-MS on an Atlantis C18 column (5 μm, 4.6×150 mm). For **9**, the mobile phase was 0.2% water, 80% acetonitrile and 19.8% MeOH flowing at 0.6 mL min^{-1} and for disulfide **10**, 4% water, 4% acetonitrile, 88% methanol and 4% of 2% formic acid in water, flowing at 0.6 mL min^{-1}. The petivericin analog **8** was quantified by its UV response (λ = 234 nm; R_t= 7.99 min) with the corresponding internal standard dodecanoic acid quantified by MS ($[M-H]^-$ = 199, R_t= 4.83 mins). For disulfide **9**, and the corresponding internal standard MS (SIR) was used (disulfide **9**: $[M-H]^-$ = 368, R_t= 5.04 mins; *N*-phenylacetamide: $[M+H]^+$ = 136, R_t= 3.18 mins).



Scheme S1. Synthesis of the lipophilic petivericin analog **8**.

(4-Hexylphenyl)methanol (S2). To a solution of hexylbenzene (1.62 g, 10 mmol) and oxalyl chloride (1.4 g, 11 mmol) in dry methylene chloride (15 mL), anhydrous $AlCl_3$ (2.0 g, 15 mmol) was added portion-wise at 0°C under argon. Anhydrous THF (10 mL) was added after the mixture was stirred at 0°C for 1 hour, and then $LiAlH_4$ (760 mg, 20 mmol) was added portion-wise. After stirring at 0°C for 1 hour, water (5 mL) was added slowly to quench the reaction. The

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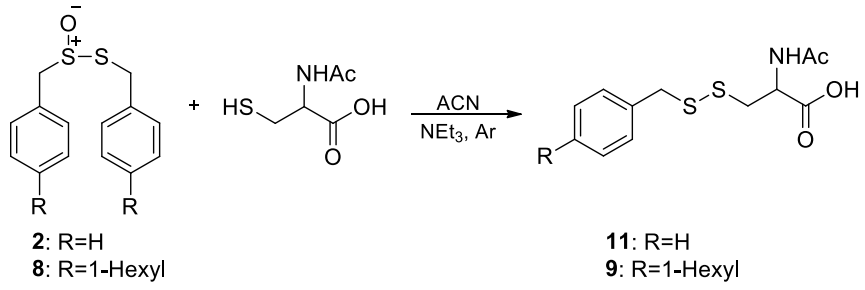
solution was then decanted, and the solid washed very well with ether. The organic solutions were combined, washed with water, brine and concentrated to give the crude product, which was purified by flash chromatography on silica gel (hexane: ethyl acetate = 5:1) to afford compound **S2** (1.73 g, 90% yield). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.06-7.18 (AB, 4H), 4.52 (s, 2H), 2.51 (t, *J*=7.5Hz, 2H), 2.18 (br, 1H), 1.52 (m, 2H), 1.16-1.29 (m, 6H), 0.80 (t, J=6.9 Hz, 3H). Spectral data are in accordance with literature values.[2]

S-4-Hexylbenzyl ethanethioate (S3). To a solution of (4-hexylphenyl)methanol **S2** (1.15 g, 6 mmol) in methylene chloride, thioacetic acid (1.37 g, 18 mmol) and ZnI_2 (954 mg, 3 mmol) were added sequentially. After refluxing overnight, the reaction was quenched with water. The organic phase was separated and the aqueous phase was extracted with ether. The organics were then combined and the solvent was removed under reduced pressure. The resulting oil was purified by flash chromatography on silica gel (hexane: ethyl acetate = 10: 1) to give compound **S3** (1.21 g, 81% yield). ^{1}H NMR (300 MHz, CDCl3): δ 6.99-7.11 (AB, 4H), 4.00 (s, 2H), 2.47(t, *J*=7.5Hz, 2H), 2.23 (s, 3H), 2.04 (m, 2H), 1.21-1.28 (m, 6H), 0.79 (t, *J*=6.6 Hz, 3H); ^{13}C NMR (75.5 MHz, CDCl3): δ 195.0, 141.9, 134.5, 128.57, 128.52, 33.5, 33.1, 31.6, 31.3, 30.2, 28.9, 22.5, 14.0; EI (M+): 250.1, HRMS (EI) calcd for $C_{15}H_{22}OS$ [M+] 250.1391, obsd 250.1357.

1,2-bis(4-hexylbenzyl)disulfane (S4). To a room temperature solution of S-4-hexylbenzyl ethanethioate **S3** (1.21 g, 4.84 mmol) in methanol (35 mL), hydrochloric acid (35-38%, 20 drops) was added. The mixture was refluxed for 10 h and then cooled down to 0^{o}C. Iodine (5% solution in methanol) was then added dropwise until the iodine colour persisted, after which the reaction was kept stirring at 0^{o}C for another 20 min. Sodium thiosulfate was added to quench the excess iodine. The mixture was concentrated under reduced pressure and the residue treated with water (15 mL) and the resulting mixture extracted with ether. The extracts were combined, dried over

magnesium sulphate and concentrated to give an oil, which was purified by flash chromatography on silica gel (hexane:ethyl acetate = 20: 1) to give compound **S4** (832 mg, 83% yield). ^{1}H NMR (300 MHz, CDCl3): δ 7.01-7.07 (AB, 8H), 3.49 (s, 4H), 2.49(t, *J*=7.5Hz, 4H), 1.50 (m, 4H), 1.15-1.27 (m, 12H), 0.78 (t, *J*=7.2 Hz, 6H); ^{13}C NMR (75.5 MHz, CDCl3): δ 142.3, 134.5, 129.4, 128.6, 43.2, 35.7, 31.8, 31.5, 29.0, 22.7, 14.2; EI (M+): 414.2, (M+/2): 207.1, HRMS (EI) calcd for $C_{26}H_{38}S_2$ [M+] 414.2415, obsd 414.2417.

S-4-hexylbenzyl (4-hexylphenyl)methanethiosulfinate (8). To a solution of 1,2-bis(4-hexylbenzyl)disulfane **S4** (909 mg, 2.19 mmol) in dichloromethane (10 mL) was added *m*-chloroperbenzoic acid (*m*-CPBA) (77%, 517 mg, 2.31 mmol) in dichloromethane (1 mL) dropwise at 0 ◦C. The mixture was stirred at 0^{o}C for one hour. Sodium carbonate (2 g) was added in small portions with vigorous stirring. The reaction mixture was stirred for an additional 1 h at 0^{o}C before being filtered through magnesium sulfate. The filtrate was concentrated under reduced pressure yielding crude product, which was recrystallized from ether to yield **8** as a white solid (575 mg, 61% yield). ^{1}H NMR (300 MHz, CDCl3): δ 7.02-7.18 (m, 8H), 4.11-4.25 (m, 4H), 2.47-2.55(m, 4H), 1.51 (m, 4H), 1.19-1.27 (m, 12H), 0.81 (m, 6H); ^{13}C NMR (75.5 MHz, CDCl3): δ 143.6, 142.6, 133.7, 128.9, 128.8, 127.1, 61.9, 35.9, 35.7, 35.6, 31.7, 31.3, 31.2, 29.0, 22.6, 14.1; HRMS (TOF MS EI+) calcd for [M^{+}-O] $C_{26}H_{38}S_2$ 414.2415, obsd 414.2403.



Scheme S2. Synthesis of mixed disulfides **9** and **11**.

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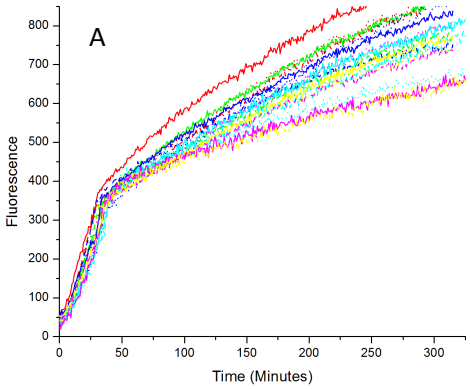
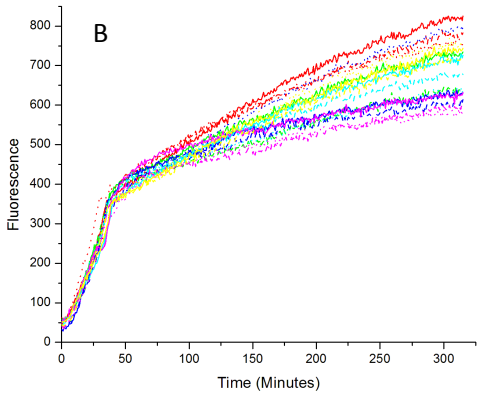
2-Acetamido-3-(benzyldisulfanyl)propanoic acid (11). To a solution of petivericin **2** (52.4 mg, 0.2 mmol) in ACN (10 mL), NAC (129 mg, 0.8 mmol) and NEt_3 (101 mg, 1 mmol) were added sequentially under argon. After stirring at room temperature overnight, the solvent was removed. The residue was diluted with water (10 mL) and the suspension extracted with Et_2O (10 mL×3). The organics were combined and the solvent removed under reduced pressure. The resulting oil was purified by flash chromatography (CH_2Cl_2:MeOH:NEt_3 =90:10:0.1) to give compound **11** (44 mg, 39% yield). ^{1}H NMR (300 MHz, MeOH-d4): δ 7.24-7.35 (m, 5H), 4.56-4.60 (m, 1H), 3.93 (AB, 2H), 2.97-3.03 (AB, 1H), 2.74-2.81 (AB, 1H), 1.99 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl3): δ 174.1, 171.9, 137.4, 129.1, 128.1, 127.0, 52.9, 42.7, 39.9, 21.2; HRMS (EI+) calcd for [M^+] $C_{12}H_{15}S_2NO_3$ 285.0493, obsd 285.0465.

2-Acetamido-3-(4-hexylbenzyldisulfanyl)propanoic acid (9). Compound **9** was prepared from compound **8** (21.5 mg, 0.05 mmol) using similar procedures as described for compound **11** giving 14 mg (41% yield.) ^{1}H NMR (300 MHz, MeOH-d4): δ 7.23-7.25 (AB, 2H), 7.11-7.14 (AB, 2H), 4.59-4.64 (m, 1H), 3.86-3.95 (AB, 2H), 2.68-2.94 (AB, 2H), 2.59 (t, *J*= 7.5 Hz, 2H), 1.99 (s, 3H), 1.57-1.62 (m, 2H), 1.29-1.35 (m, 6H), 0.89 (t, *J*= 7.2 Hz, 3H) ; ^{13}C NMR (75.5 MHz, CDCl3): δ 172.7, 171.8, 141.9, 134.4, 128.9, 128.1, 51.8, 42.5, 39.3, 35.2, 31.4, 31.2, 28.6, 22.2, 21, 12.9; HRMS (TOF MS EI+) calcd for $C_{18}H_{27}S_2NO_3$ 369.1432, obsd 369.1443.


A
Fluorescence
Time (Minutes)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Fluorescence
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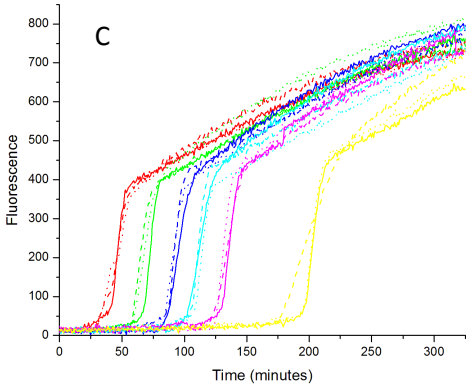
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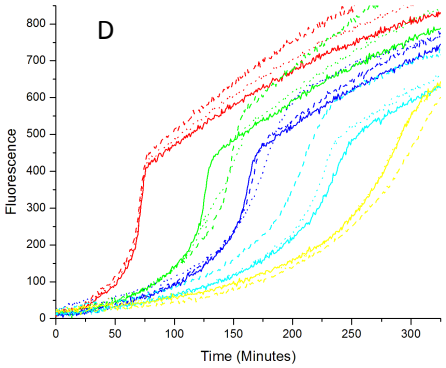
Fluorescence
Time (minutes)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Fluorescence
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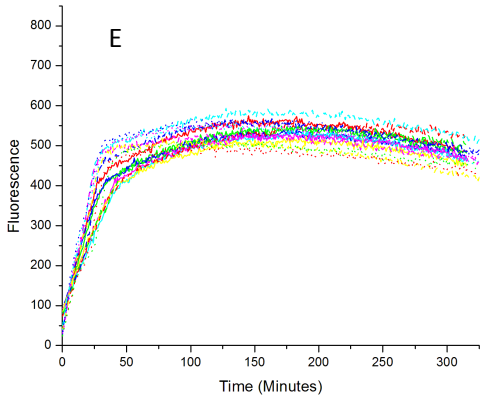
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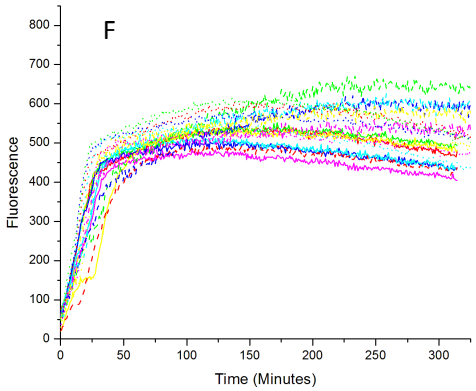
Time (Minutes)


F
Fluorescence
Time (Minutes)

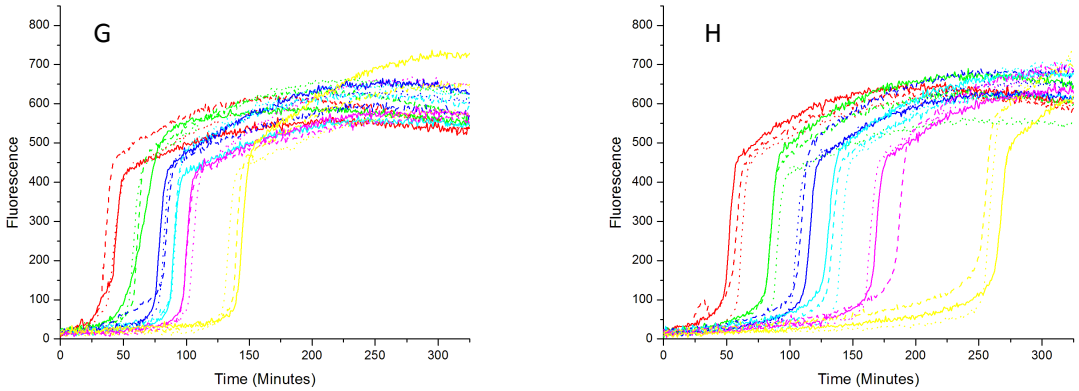


Figure S1. Fluorescence intensity−time profiles (recorded from three separate experiments) from MeOAMVN (0.2 mM)-mediated (A, B, C, D) or ABAP (2.7 mM)-mediated (E, F, G, H) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM H_2B-PMHC and increasing concentrations (1.5 μM - red, 3.0 μM - green, 4.5 μM - blue, 6.0 μM - cyan, 7.5 μM - magenta and 15 μM - yellow) of **1** (A, E), **2** (B, F), **5** (C, G) and **7** (D, H). Fluorescence at 520 nm was recorded every 50 s.

A kinetic analysis based on the initial rates of H_2B-PMHC oxidation in the presence and absence of added antioxidant has been carried out to provide an expression useful for the quantification of the relative rate constants in this competition[3]:

$$\ln\left(\frac{I_\infty - I_t}{I_\infty - I_0}\right) = \frac{k_{inh}^{\mathrm{H2B-PMHC}}}{k_{inh}^{\mathrm{unknown}}} \ln(1 - \frac{t}{\tau})$$

Thus, from a plot of $\ln[(I_\infty - I_t)/(I_\infty - I_0)]$ vs $\ln(1\text{-}t/\tau)$ (e.g. Figure S2), the relative rate constant can be determined and are given for the various concentrations of **5** and **7** in Table S1.

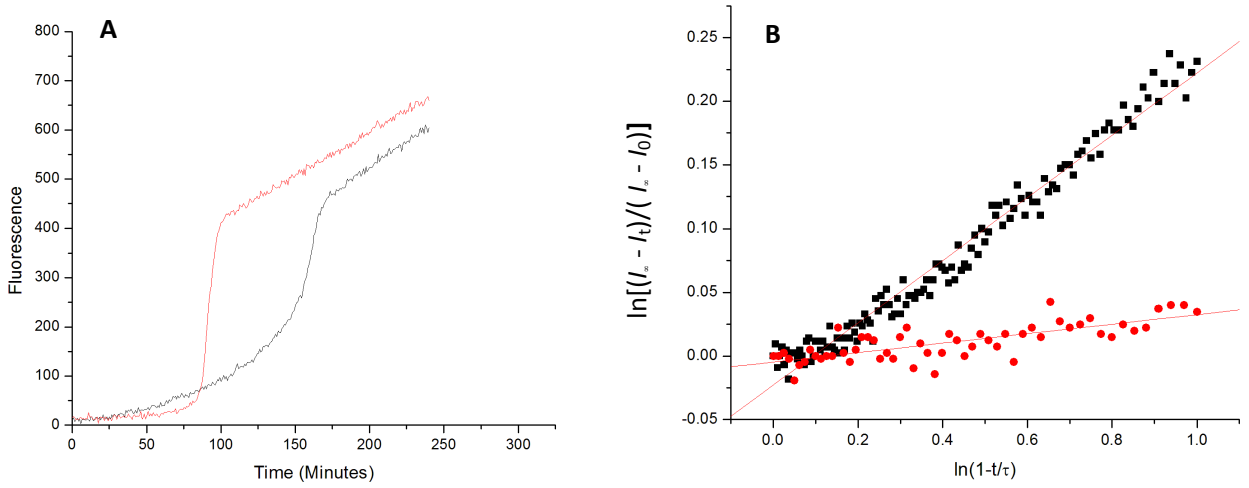


Figure S2. (A) Fluorescences (at 520 nm) intensity-time profiles from MeOVANM-mediated (0.2 mM) oxidations of egg phosphatidylcholine liposomes (1 mM in PBS buffer, pH 7.4) containing 0.15 μM H_2B-PMHC and 4.5 μM of **5** (red), PMHC (black). (B) The data in (A) plotted according to Eq. (8) for **5** (red) and PMHC (black).

Table S1. Relative rate constants for the reactions of persistent sulfenic acid **5** and PMHC (**7**) with MeOAMVN-derived peroxyl radicals derived from data in Figure 1C and 1D.

[Antioxidant]	$k_{inh}^{H2B\text{-}PMHC}/k_{inh}^{5}$	$k_{inh}^{H2B\text{-}PMHC}/k_{inh}^{7}$	k_{inh}^{5}/k_{inh}^{7}
1.5	0.037	0.22	5.9
3.0	0.039	0.21	5.4
4.5	0.033	0.24	7.3
6.0	0.040	0.22	5.5
7.5	0.033	0.20	6.1
15	0.030	0.22	7.3
average	**0.035±0.004**	**0.22±0.01**	**6.3±0.8**

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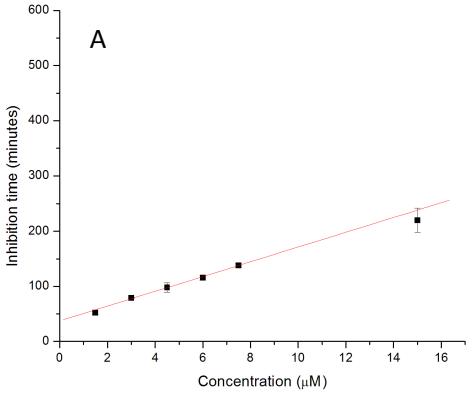
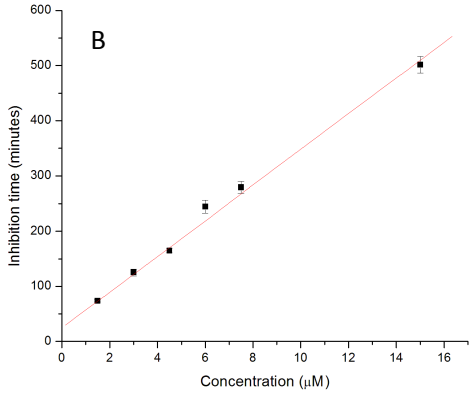
Table S2. Relative rate constants for the reactions of persistent sulfenic acid **5** and PMHC (**7**) with AAPH-derived peroxyl radicals derived from data in Figure S1C and S1D.

[Antioxidant]	$k_{inh}^{H2B\text{-}PMHC}/k_{inh}^{5}$	$k_{inh}^{H2B\text{-}PMHC}/k_{inh}^{7}$	k_{inh}^{5}/k_{inh}^{7}
1.5	0.048	0.089	1.9
3.0	0.043	0.085	2.0
4.5	0.037	0.088	2.4
6.0	0.042	0.083	2.0
7.5	0.038	0.090	2.4
15	0.033	0.086	2.6
average	**0.040±0.005**	**0.089±0.003**	**2.2±0.3**





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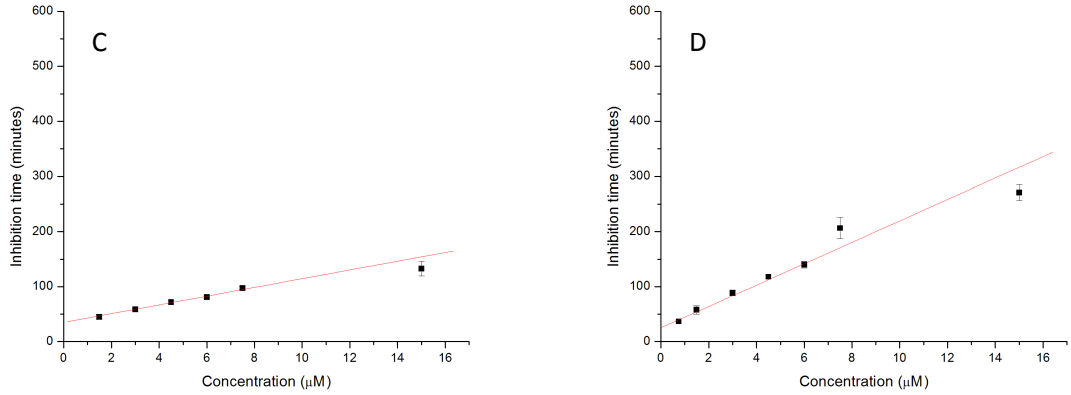


Figure S3. The inhibition time of MeOAMVN-mediated (0.2 mM, A, B) and ABAP-mediated (2.7 mM, C, D) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM of H_2B-PMHC and either **5** (A, C) or **7** (B, D) at 1.5, 3, 4.5, 6, 7.5, 15 μM.

It should be pointed out that the rate of radical generation can be derived from the inhibited times given above for the various concentrations of PMHC (whose stoichiometry for reactions with peroxyl radicals in lipid bilayers is known to be 2, as referred to in the manuscript). For example, for MeOAMVN, the data for PMHC in Fig. 1D yields R_i = 0.88±0.09 nM/s, which is in excellent agreement with the expected value of 1.2 nM/s from the kinetic data reported in reference 17 of the manuscript. Likewise for ABAP, the data for PMHC in Fig. S1D yields R_i = 1.3±0.3 nM/s, which compares well with the expected value of 0.89 nM/s from the kinetic data reported in reference 18 of the manuscript.

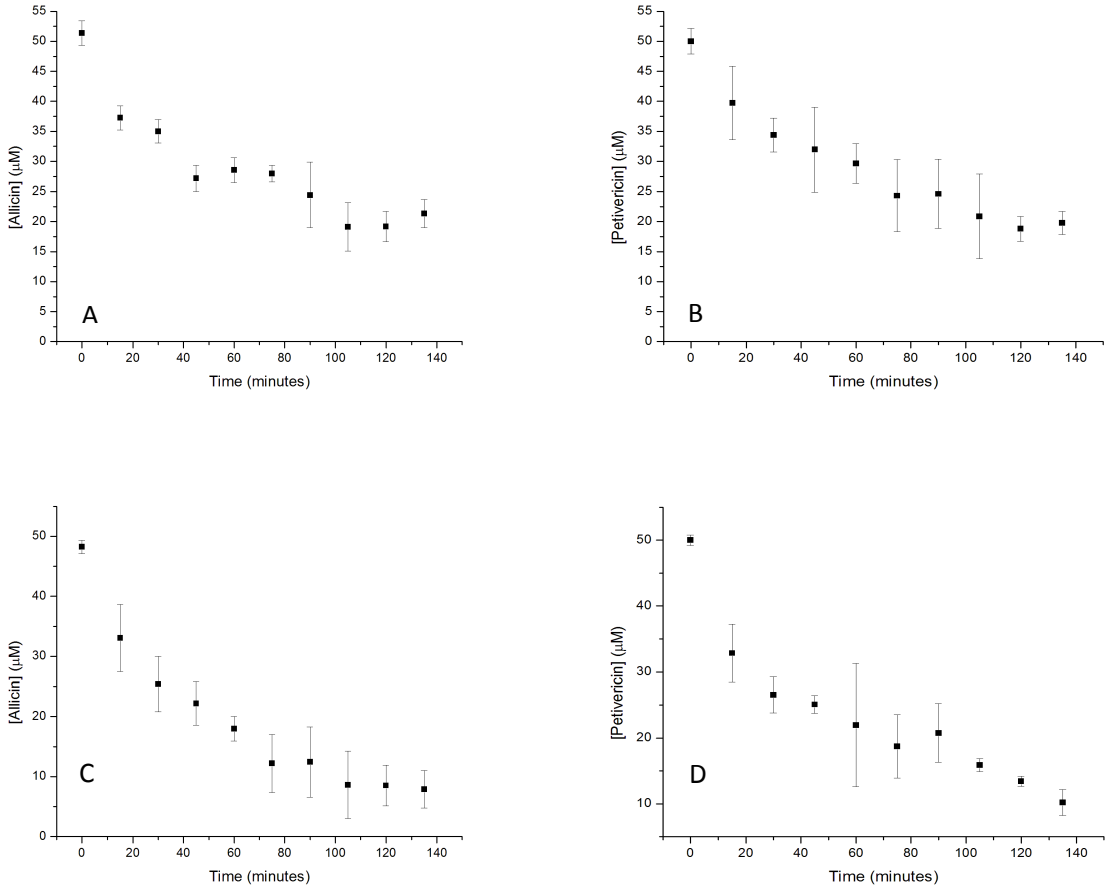


Figure S4. Decomposition of 50 μM allicin **1** without MeOAMVN (A) or with 0.2 mM MeOAMVN and 0.15 μM H_2B-PMHC (C); and Decomposition of 50 μM petivericin **2** without MeOAMVN (B) or with 0.2 mM MeOAMVN and 0.15 μM H_2B-PMHC (D), in unilamellar phosphatidylcholine liposomes

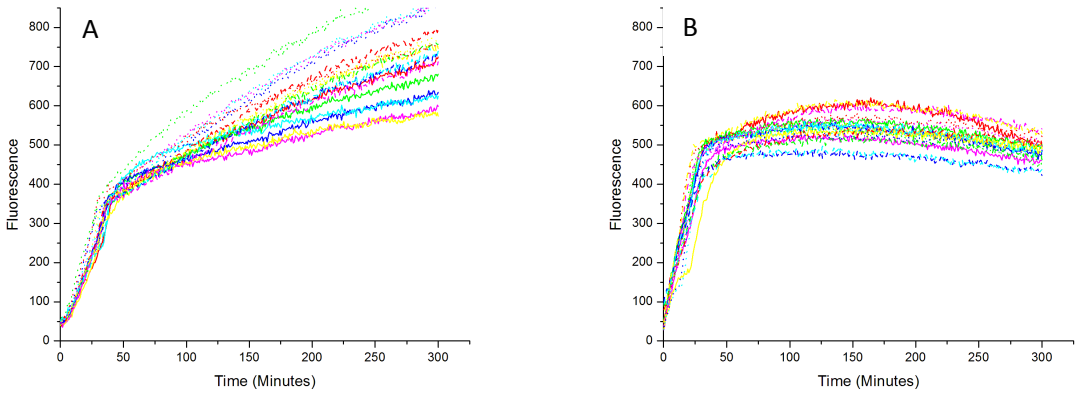


Figure S5. Fluorescence intensity−time profiles (recorded from three separate experiments) from MeOAMVN-mediated (0.2mM, A) or ABAP-mediated (2.7 mM, B) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM H_2B-PMHC and increasing concentrations (1.5 μM - red, 3.0 μM - green, 4.5 μM - blue, 6.0 μM - cyan, 7.5 μM - magenta and 15 μM - yellow) of **8**. Fluorescence at 520 nm was recorded every 50 s.

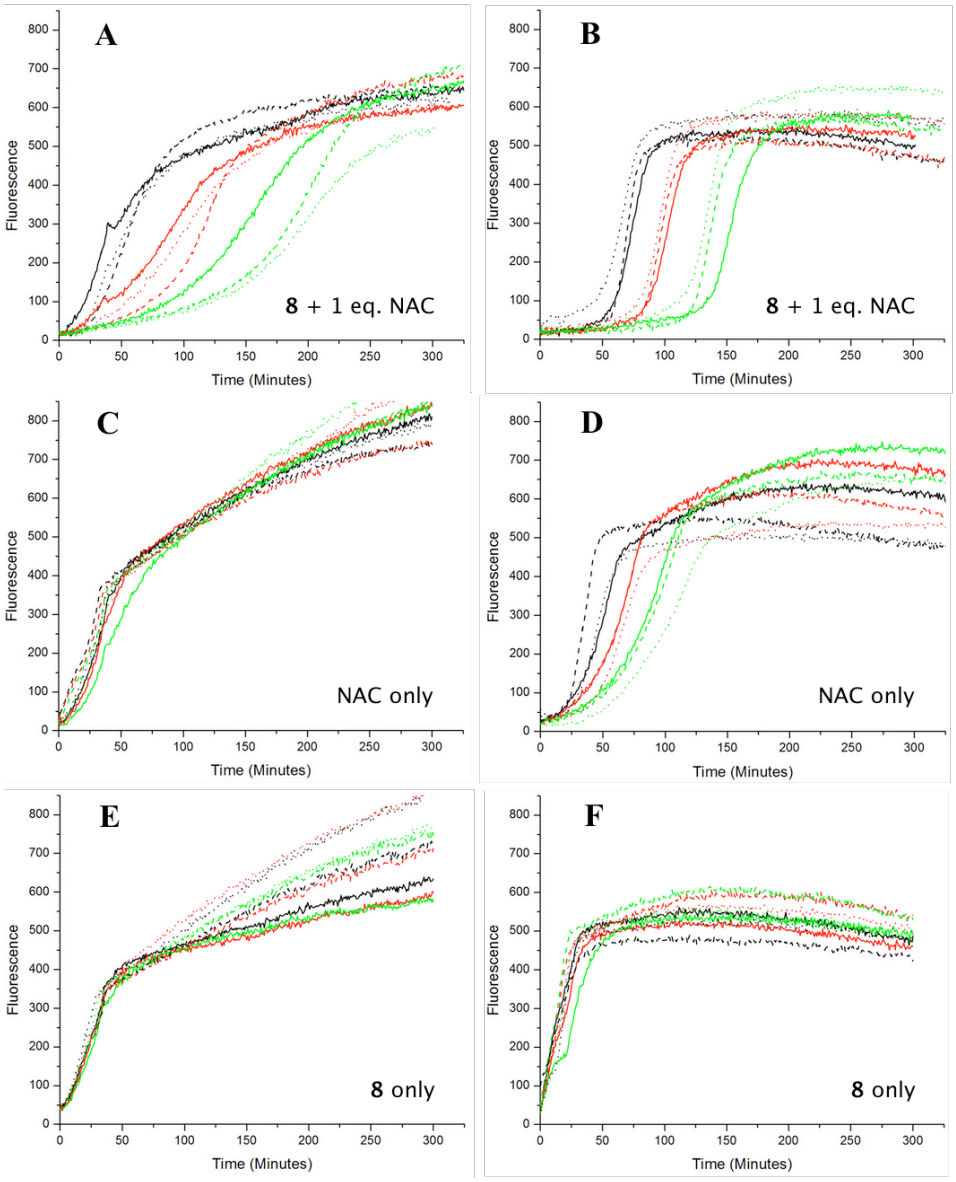


Figure S6. Fluorescence (at 520 nm) intensity-time profiles (recorded from three separate experiments) from MeOAMVN-mediated (0.2 mM, left) and ABAP-mediated (2.7 mM, right) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM **6** and either 4.5 μM (black), 7.5 μM (red) or 15 μM (green) **8** and/or an equivalent of NAC in PBS buffer of pH 7.4.

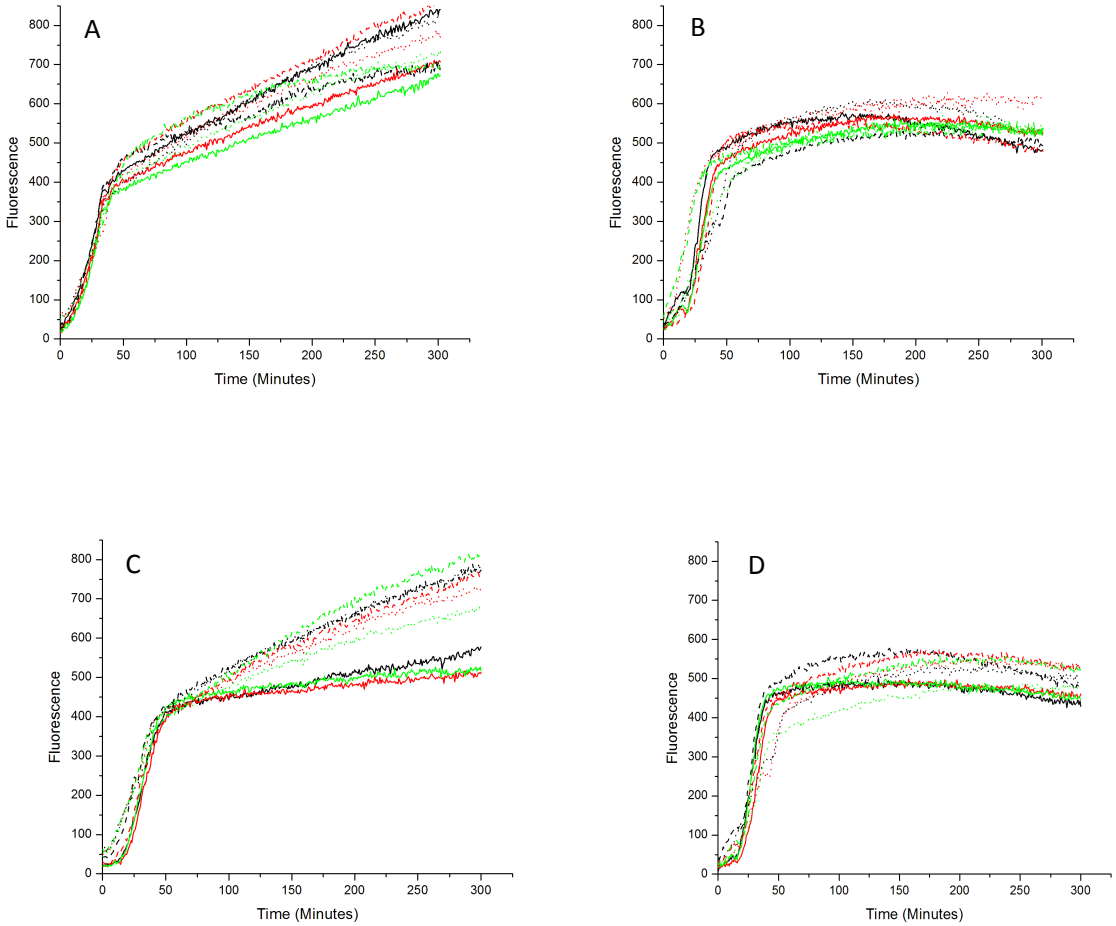


Figure S7. Fluorescence intensity−time profiles (recorded from three separate experiments) from MeOAMVN-mediated (0.2mM, A,C) or ABAP-mediated (2.7 mM, B,D) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM H_2B-PMHC and either allicin **1** (A,B) or petivericin **2** (C,D) at 4.5 μM (black), 7.5 μM (red) or 15 μM (green) in PBS buffer of pH 7.4 containing an equivalent amount of NAC. Fluorescence at 520 nm was recorded every 50 s.

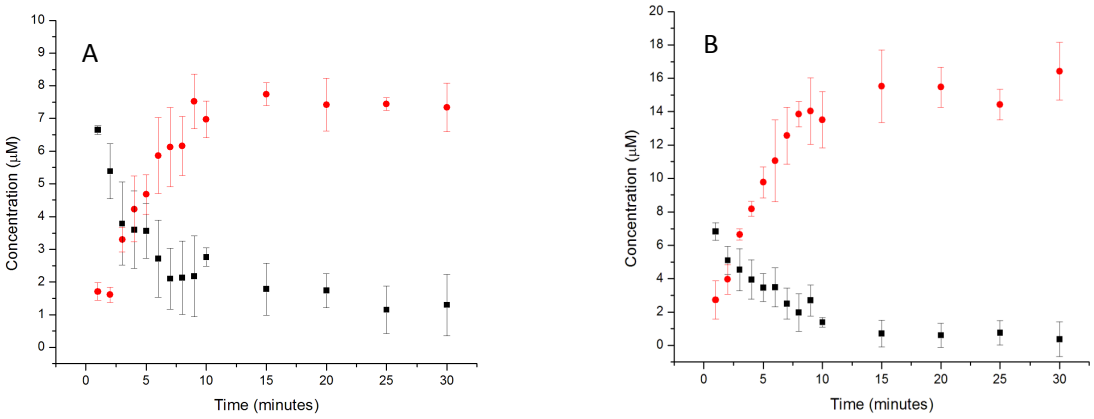


Figure S8. Decomposition of 7.5 μM petivericin **2** (■) in MeOAMVN-mediated (0.2 mM) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM H2B-PMHC and either 7.5 μM (A) or 15 μM NAC (B) in PBS buffer of pH 7.4 and formation of the corresponding mixed disulfide **11** (●).

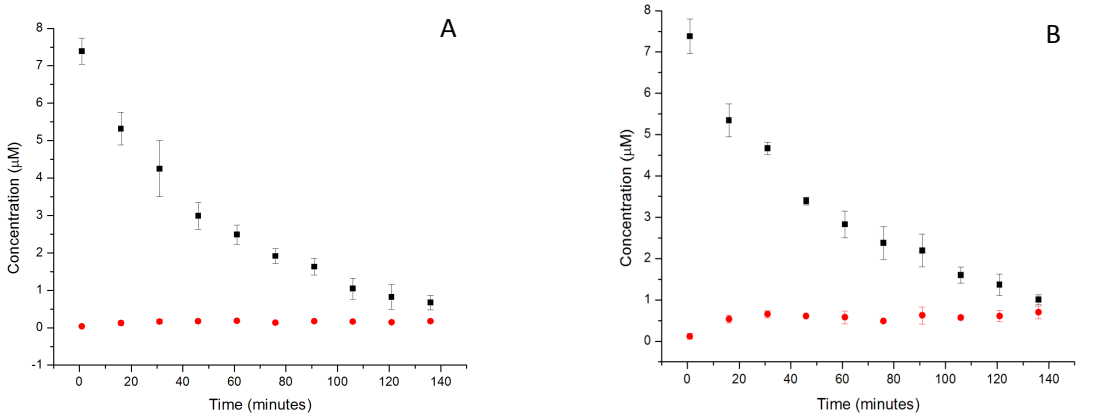


Figure S9. Decomposition of 7.5 μM *para-n*-hexylpetivericin **8** (■) in MeOAMVN-mediated (0.2 mM) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM H2B-PMHC and 7.5 μM (A) or 15 μM NAC (B) in PBS buffer of pH 7.4 and formation of the corresponding mixed disulfide **9** (●).

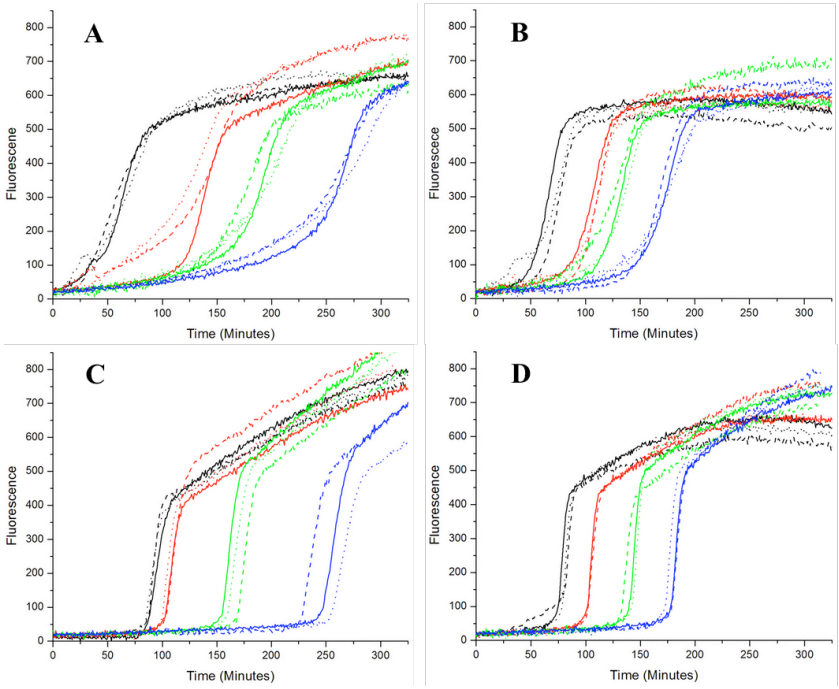
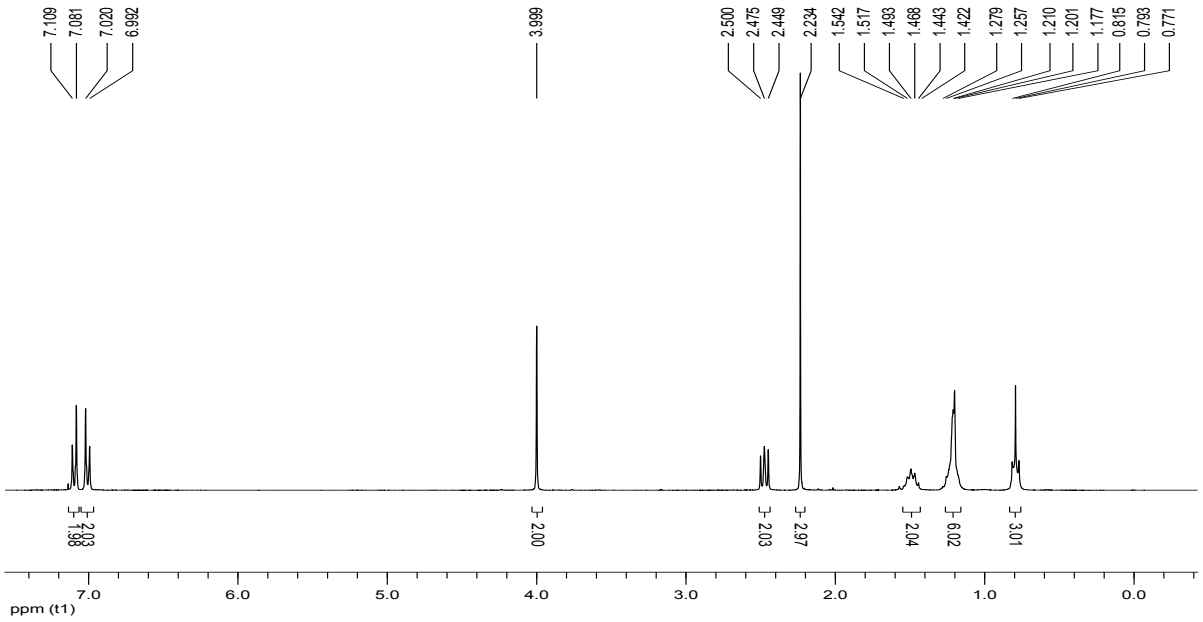


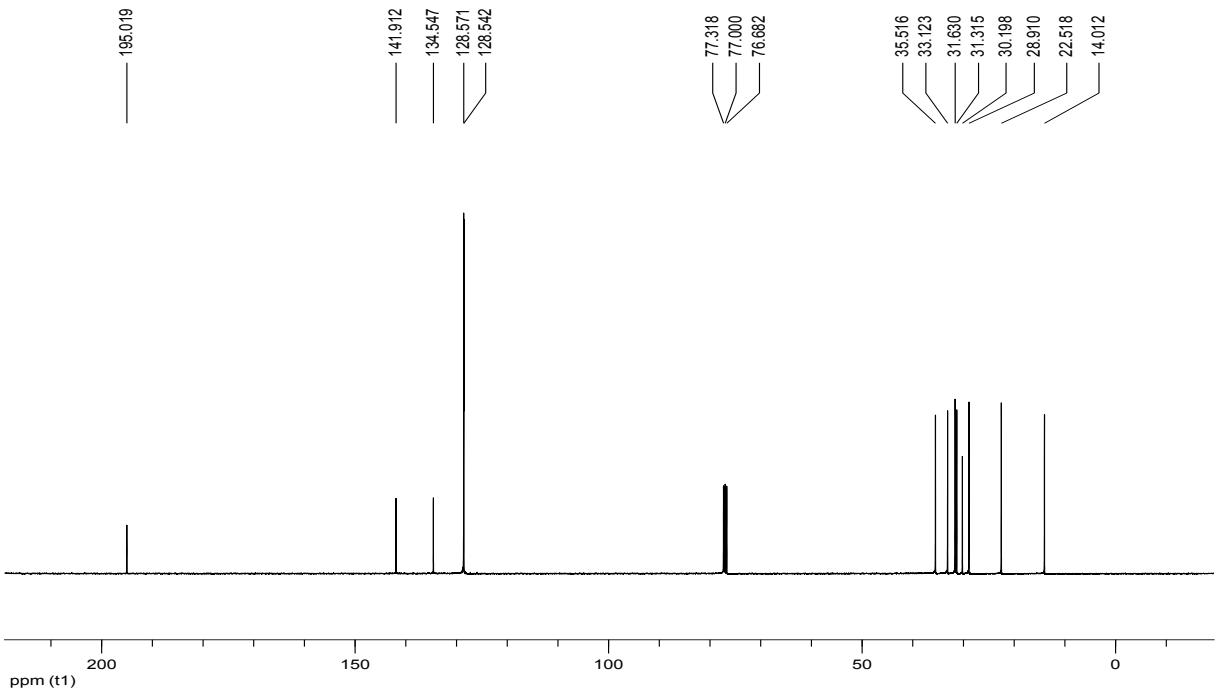
Figure S10. Representative fluorescence (at 520 nm) intensity-time profiles from MeOAMVN-mediated (0.2 mM, left) and ABAP-mediated (2.7 mM, right) oxidations of egg phosphatidylcholine liposomes (1 mM) containing 0.15 μM H_2B-PMHC and either 4.5 μM **8** (A, B) with 1, 2, 3 or 5 eq. of NAC, or 4.5 μM **5** (C, D) with 0, 1, 2 or 4 eq. of NAC.

S-4-hexylbenzyl ethanethioate (**S3**)

^{1}H NMR

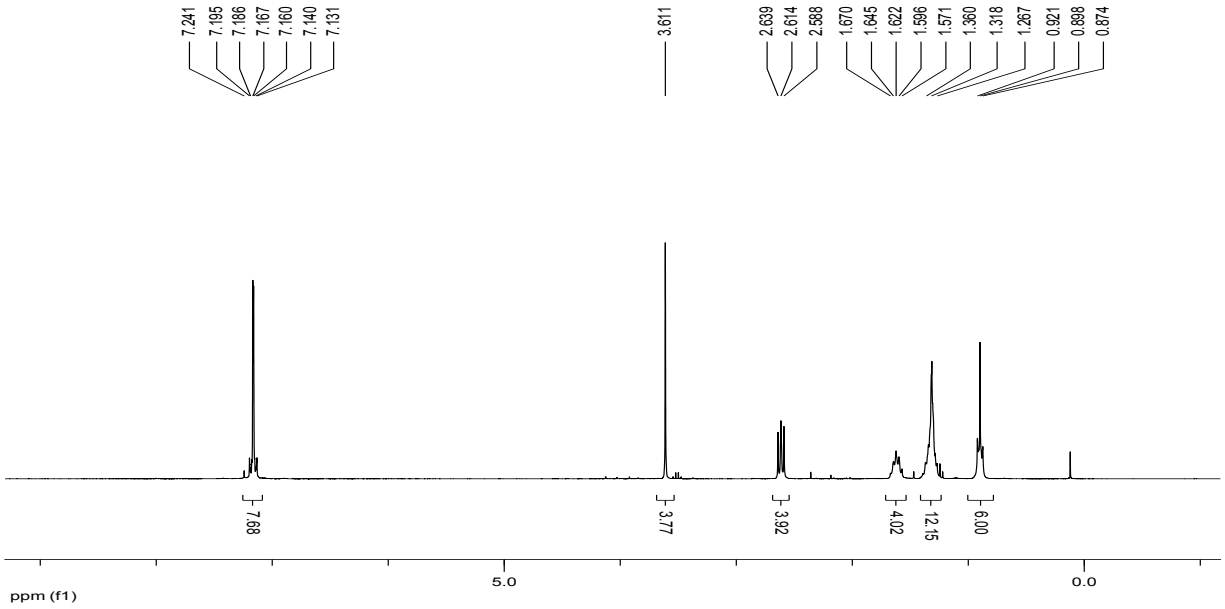


^{13}C NMR

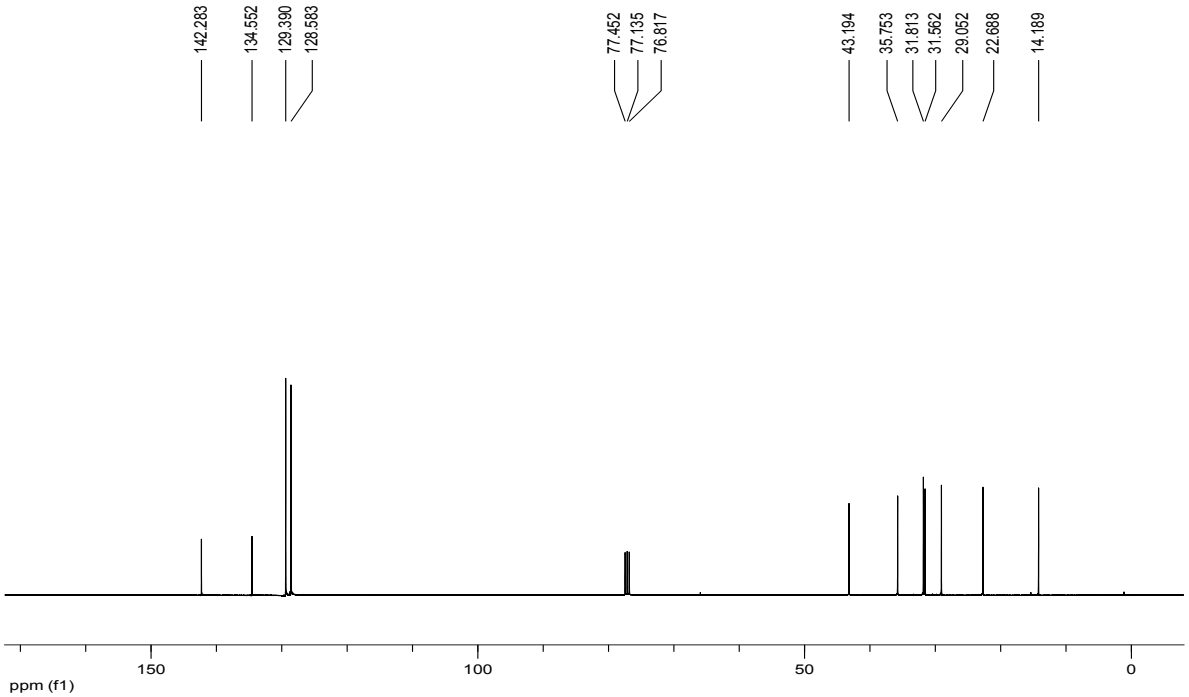


1,2-bis(4-hexylbenzyl)disulfane (**S4**)

^{1}H NMR

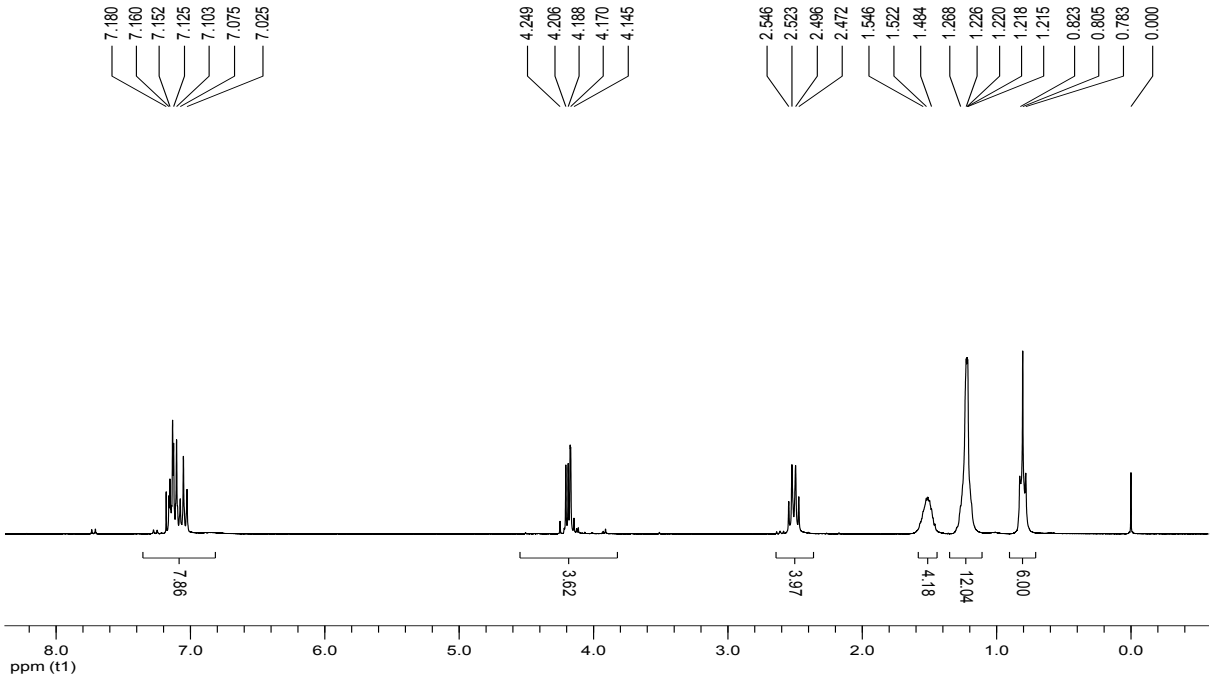


^{13}C NMR

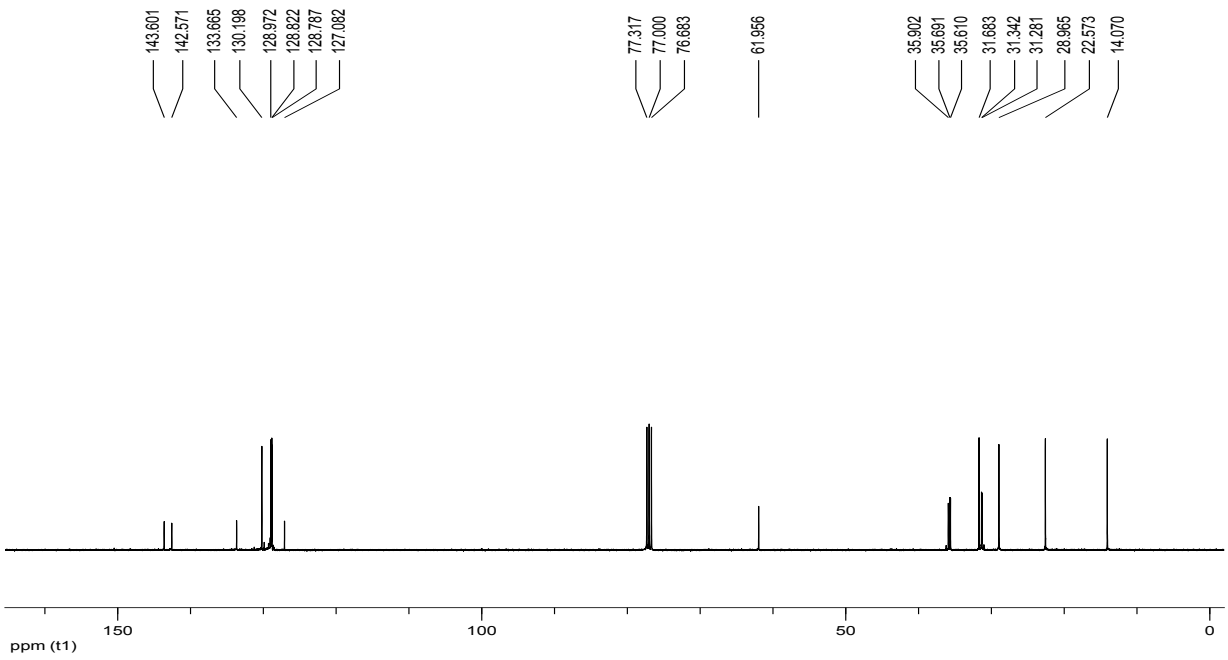


S-4-hexylbenzyl (4-hexylphenyl)methanethiosulfinate (**8**).

^{1}H NMR

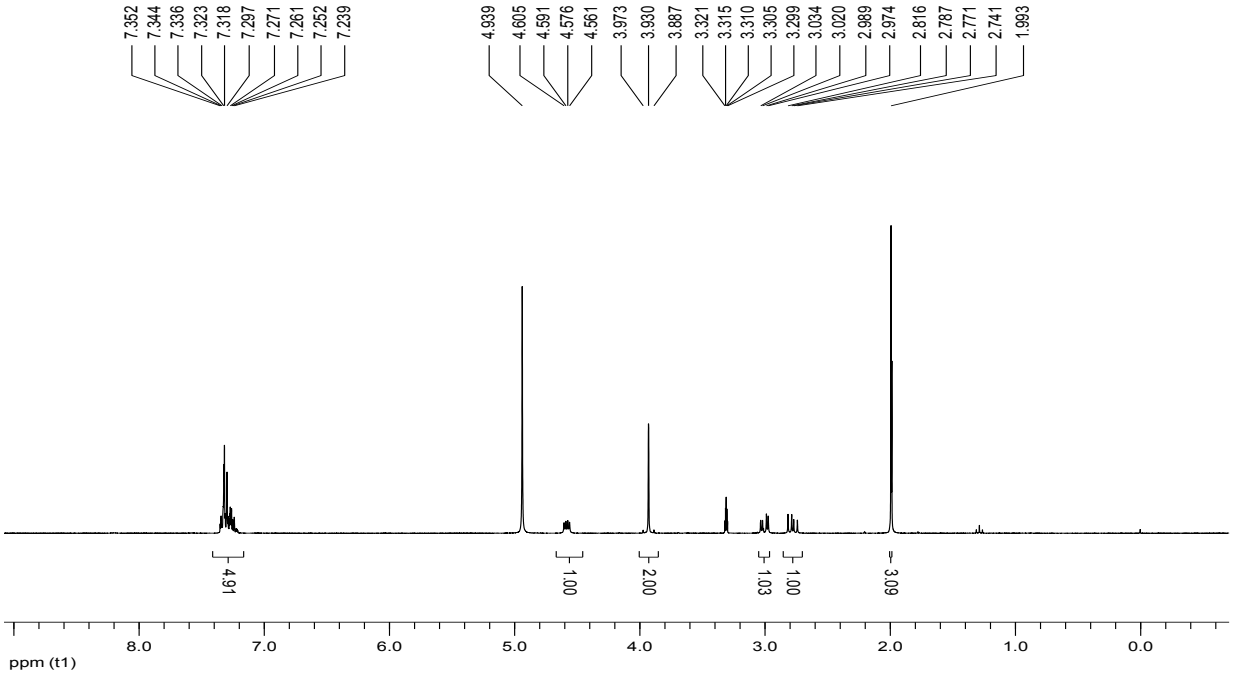


^{13}C NMR

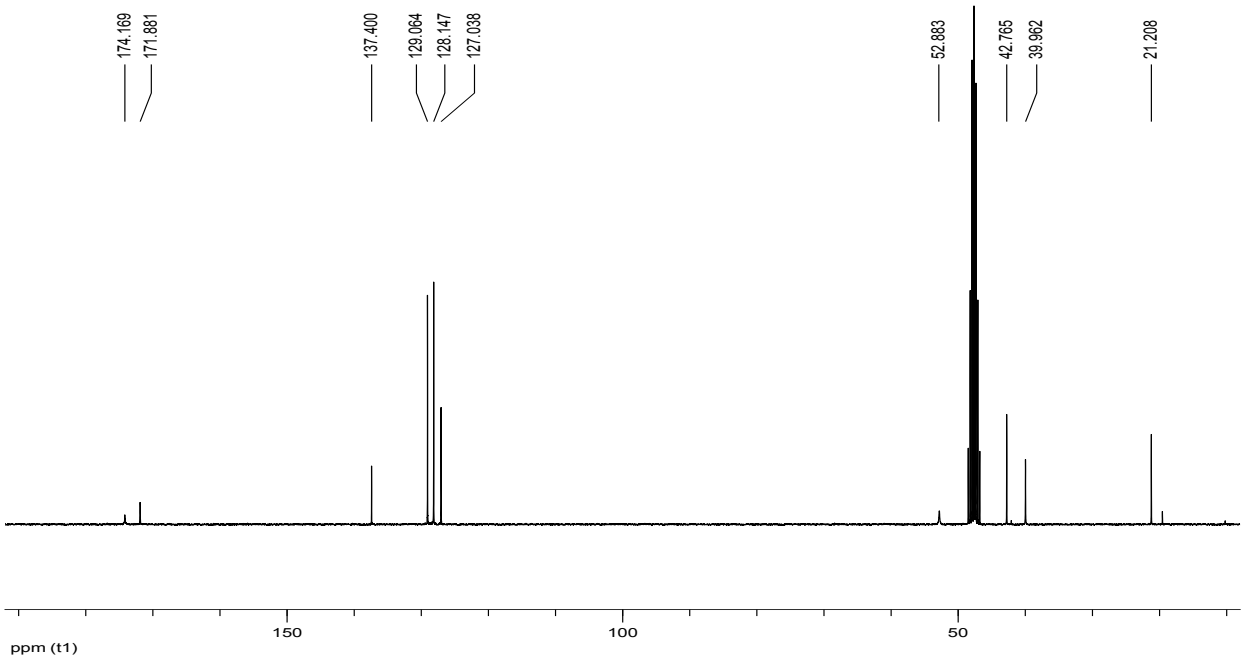


2-acetamido-3-(benzyldisulfanyl)propanoic acid (**11**)

^{1}H NMR

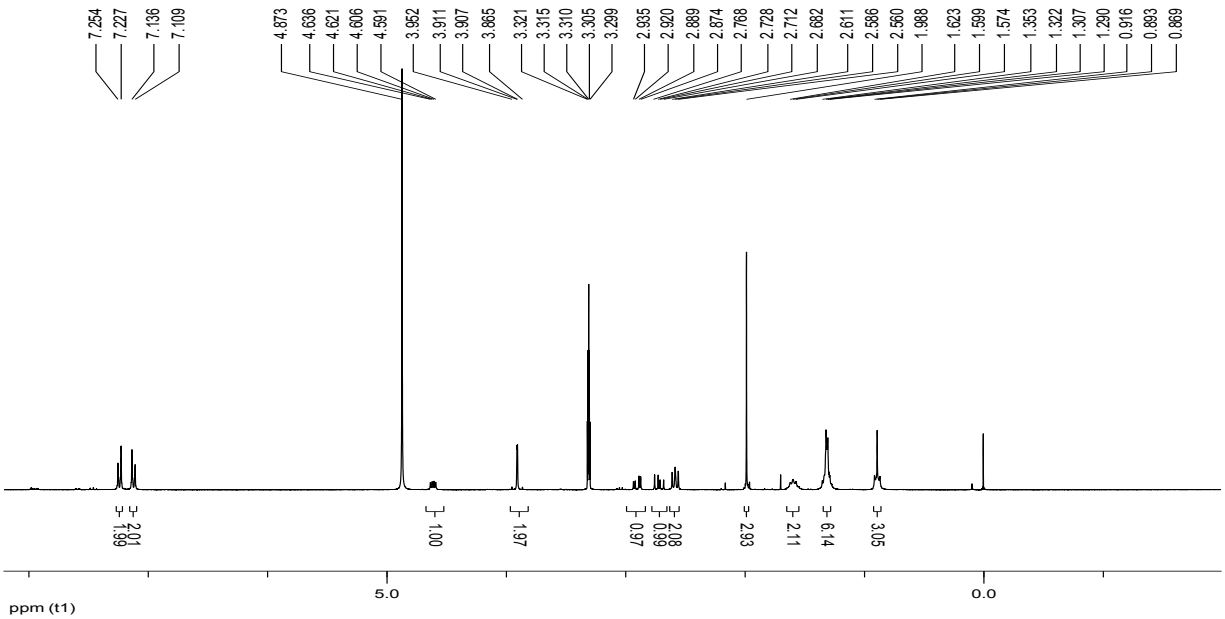


^{13}C NMR

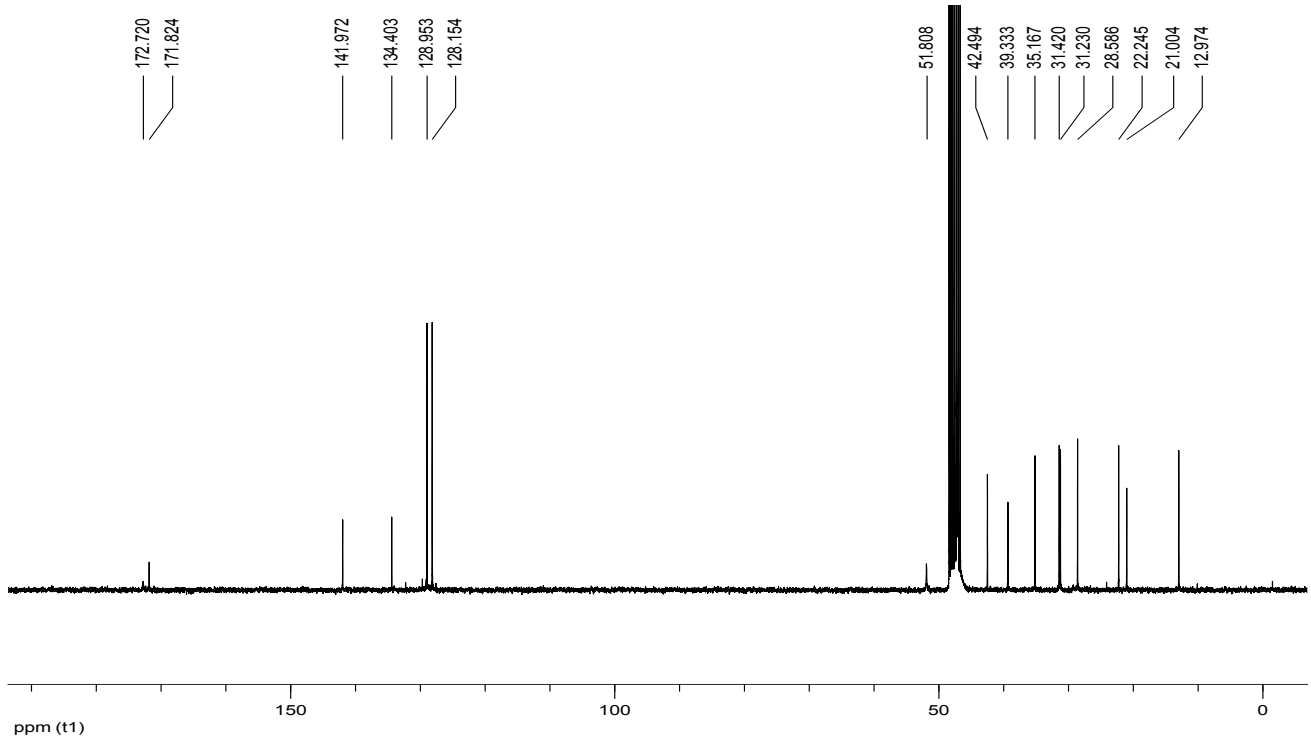


2-Acetamido-3-((4-hexylbenzyl)disulfanyl)propanoic acid (**9**)

^{1}H NMR



^{13}C NMR



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