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Supplementary Materials

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Received: 30 August 2020; Accepted: 22 September 2020; Published: date

Abstract: Cancer is a serious health burden on global societies. The discovery and development of new anti-cancer therapies remains a challenging objective. Although it has been shown that lichen secondary metabolites may be potent sources for new anti-cancer agents, the Indonesian- grown folious lichens, *Physcia millegrana, Parmelia dilatata* and *Parmeila aurulenta,* have not yet been explored. In this study exhaustive preparative high-performance liquid chromatography was employed to isolate the lichen constituents with spectroscopic and spectrometric protocols identifying nine depsides **9–17**, including the new methyl 4-formyl-2,3-dihydroxy-6-methylbenzoate **13**. The cytotoxicity of the depsides towards cancer cells was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The results indicated lowest toxicity of the depsides towards human A549 lung cancer cells. Importantly, the di-depsides (**11**, **12** and **17**) showed greatest toxicity, indicating that these structures are biologically more active than the mono-depsides against the HepG2 liver cancer, A549 lung cancer and HL-60 leukemia cell lines.

Keywords: Indonesia; lichen; *Physcia millegrana*; *Parmelia dilatata*; *Parmelia aurulenta*; depsides; anti-cancer

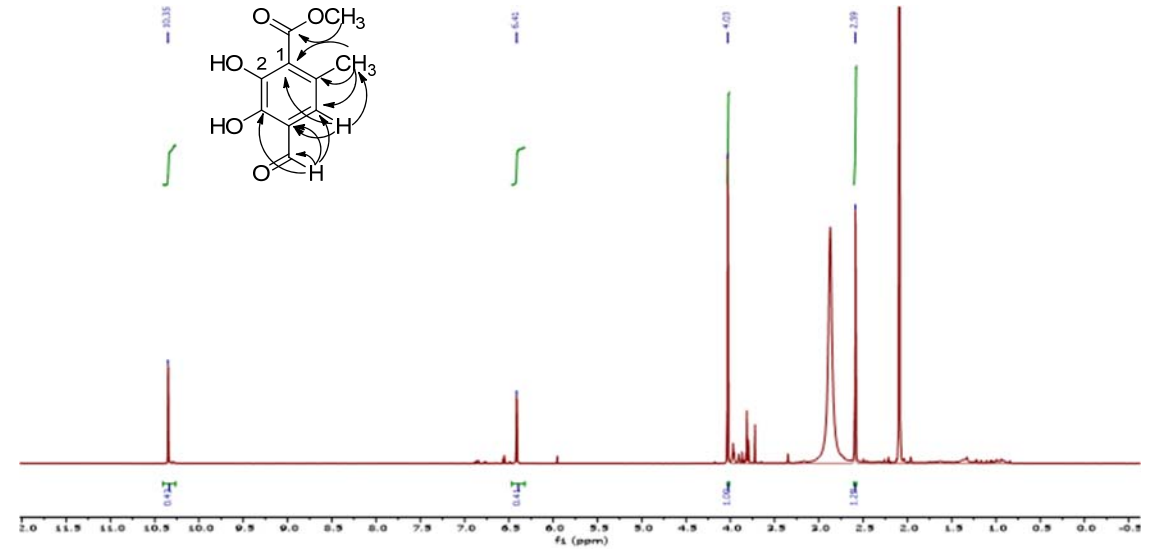

Figure S1. [1]H-NMR spectrum of compound **13** in acetone-*d6*.

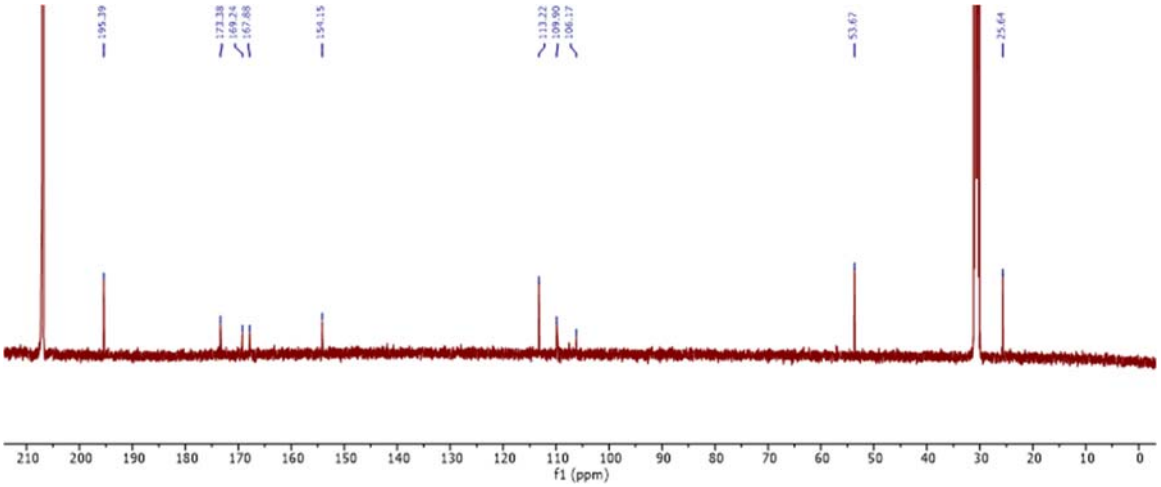

Figure S2. [13]C-NMR spectrum of compound **13** in acetone-*d6*.

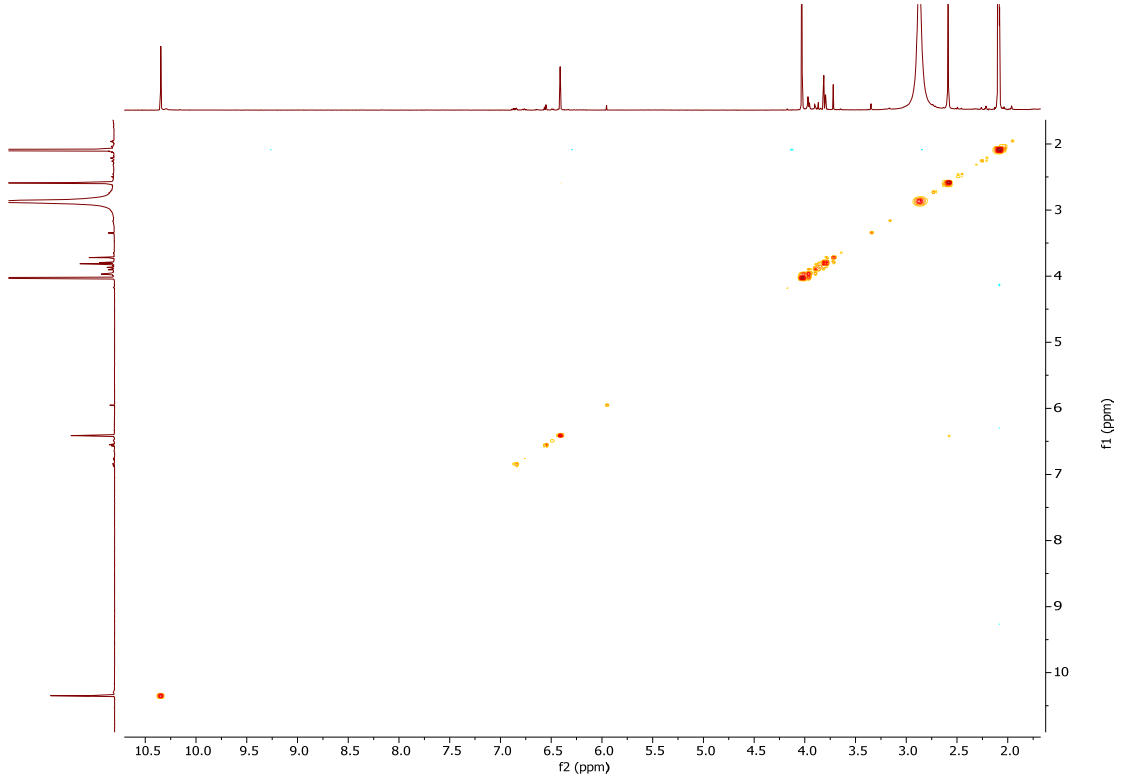

Figure S3. gCOSY-NMR spectrum of compound **13** in acetone-*d6*.

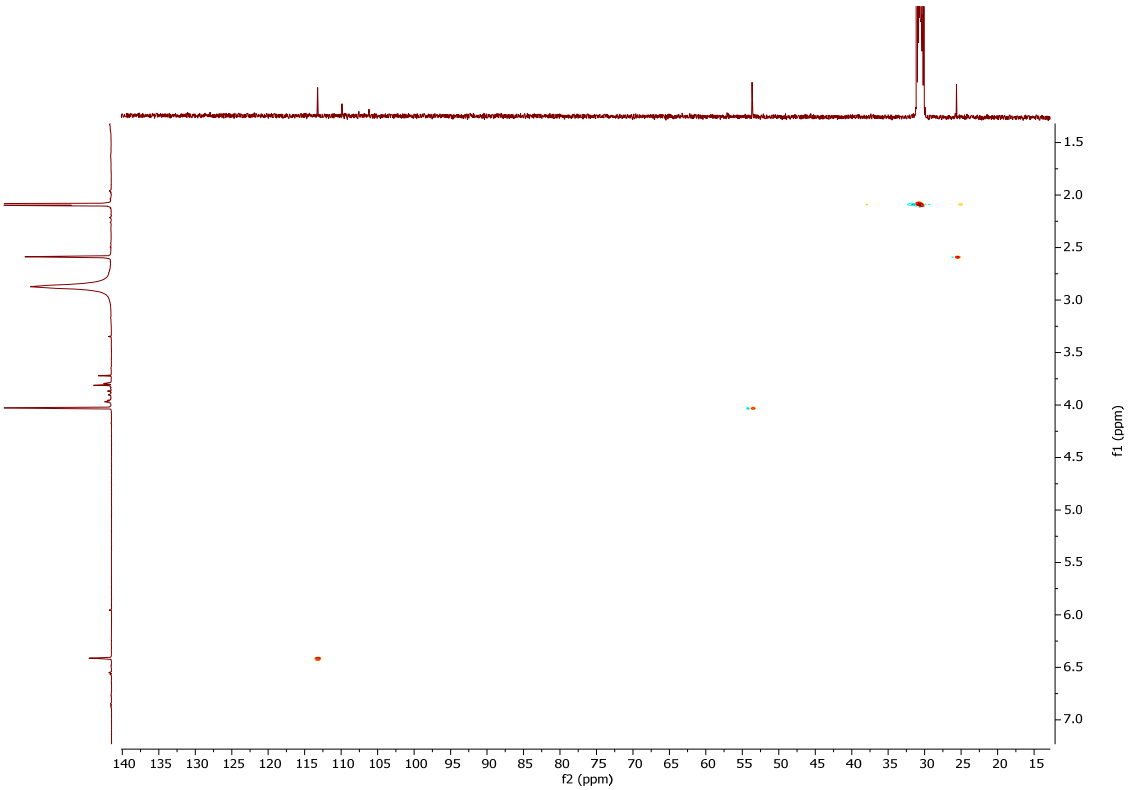

Figure S4. gHSQC-NMR spectrum of compound **13** in acetone-*d6*.

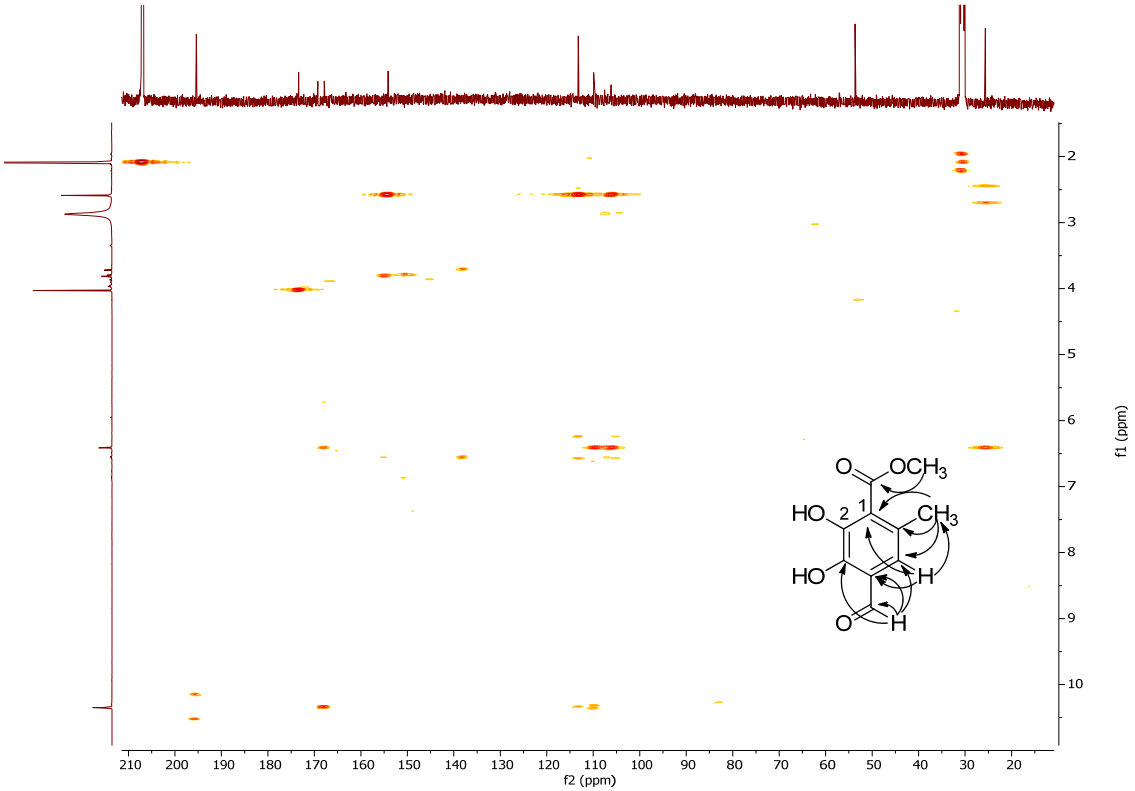

Figure 5. gHMBC-NMR spectrum of compound **13** in acetone-*d6*.

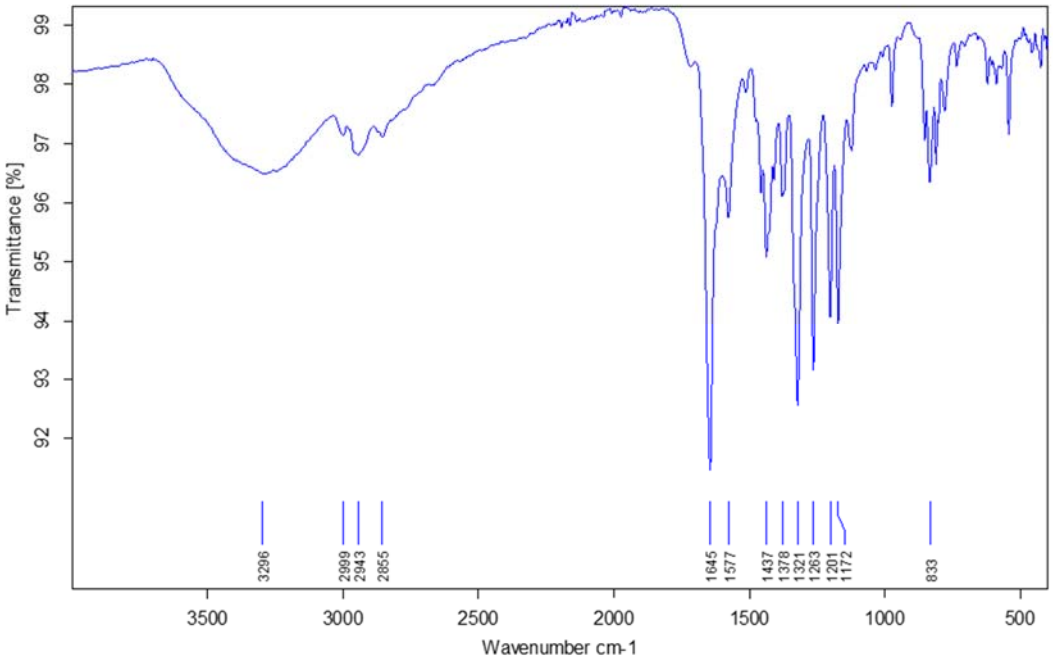

Figure S6. IR spectrum of compound **13.**

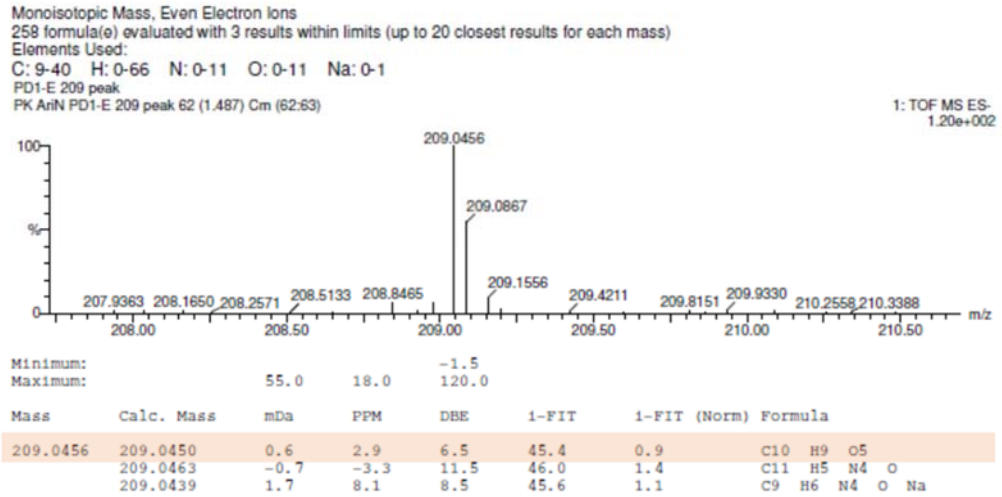

Figure S7. HRESI spectrum of compound **13.**

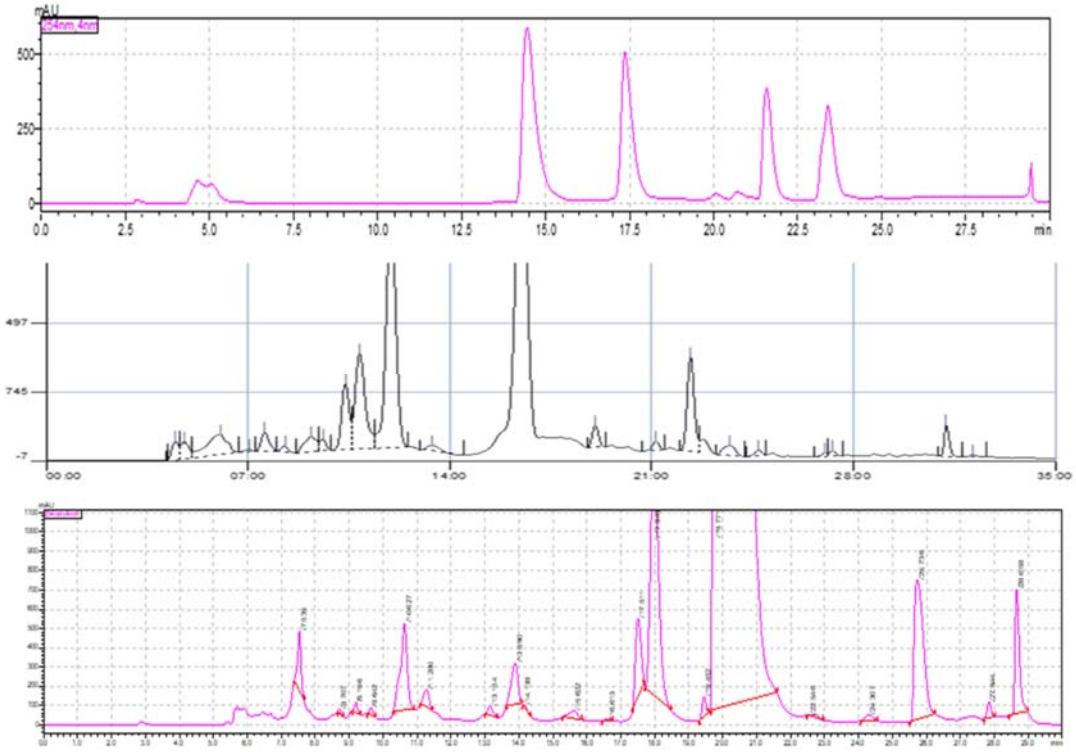

Figure S8. Chromatogram of preparative HPLC of *Pysicia millegrana* (top), *Parmelia dilatata* (middle) and *Parmelia aurulenta* (bottom).

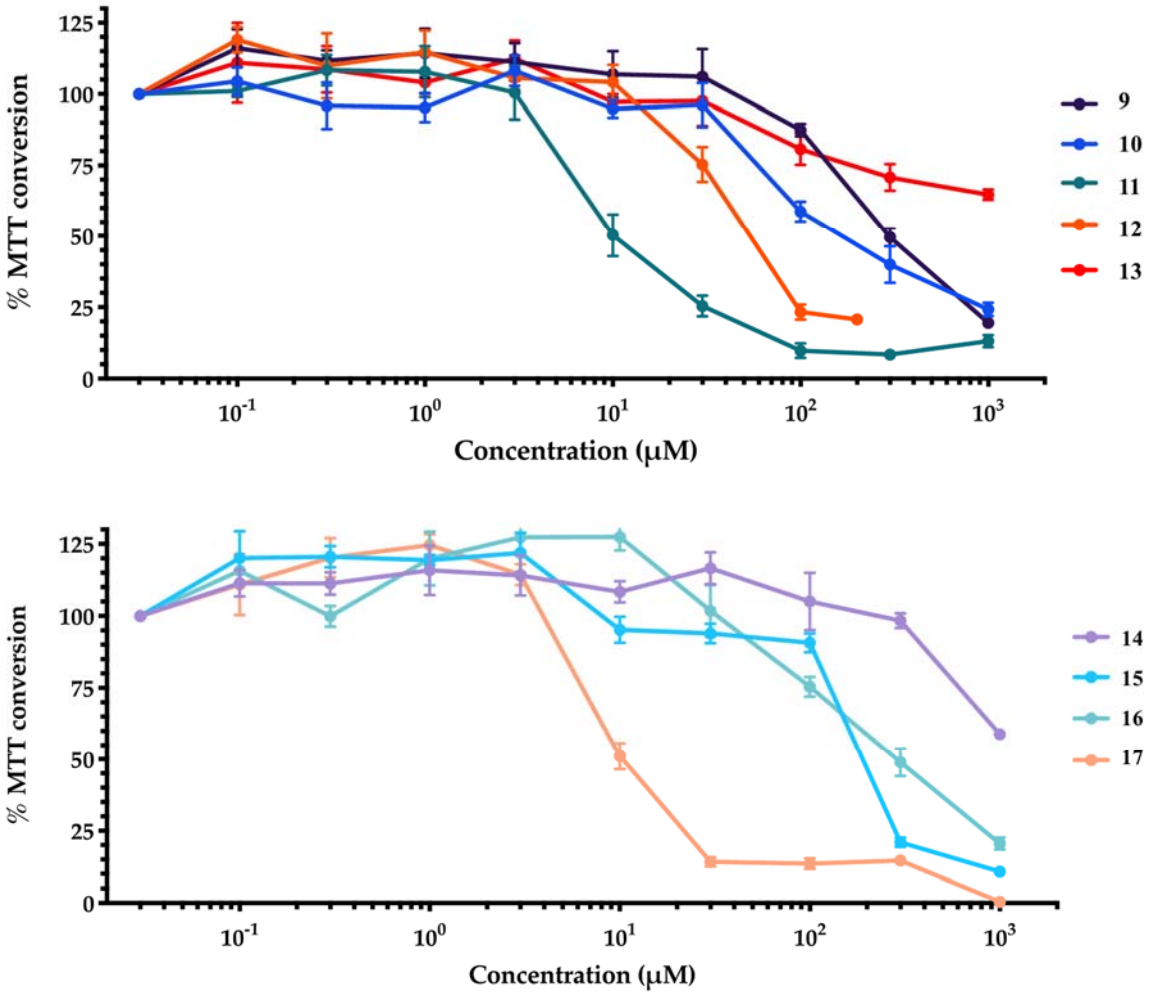

Figure S9. Concentration-response curves for the MTT assay of the specified compounds tested against HepG2 cells. The data points represent the mean of 6 points and the error bars represent the standard deviation from the mean.

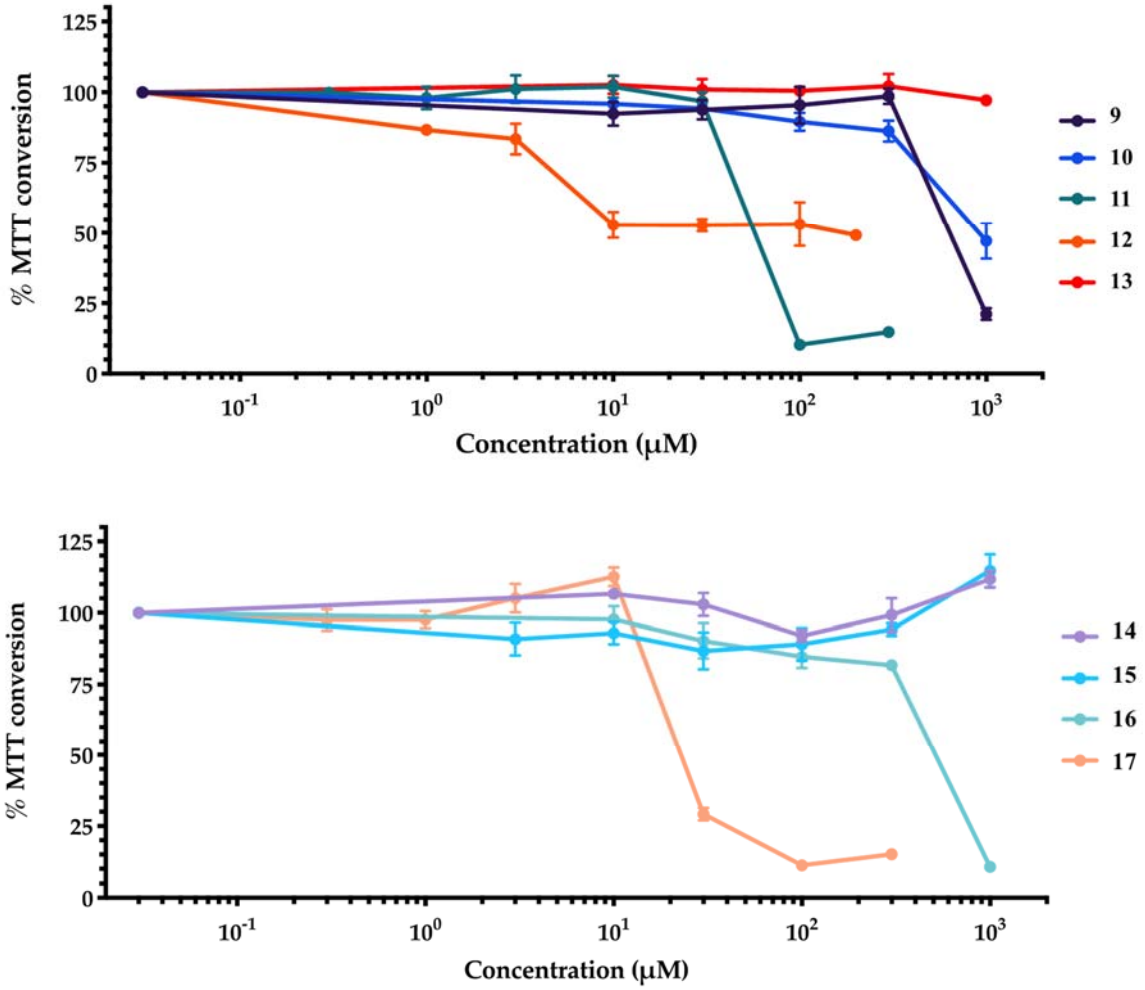

Figure S10. Concentration-response curves for the MTT assay of the specified compounds tested against A549 cells. The data points represent the mean of 6 points and the error bars represent the standard deviation from the mean.

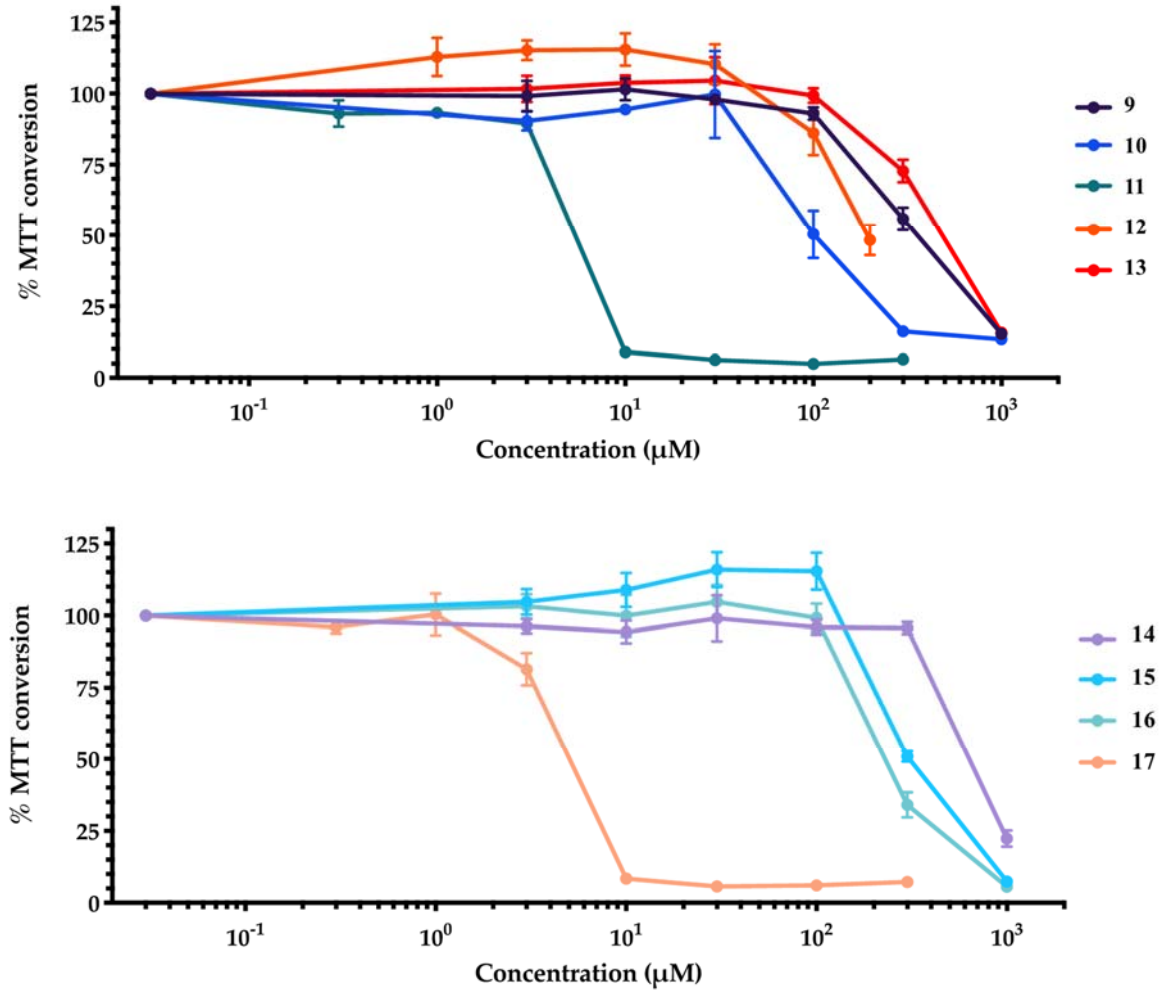

Figure S11. Concentration-response curves for the MTT assay of the specified compounds tested against HL60 cells. The data points represent the mean of 6 points and the error bars represent the standard deviation from the mean.