Supporting Informations

An original and efficient antibiotic adjuvant strategy to enhance the activity of macrolide antibiotics against Gram-negative resistant strains

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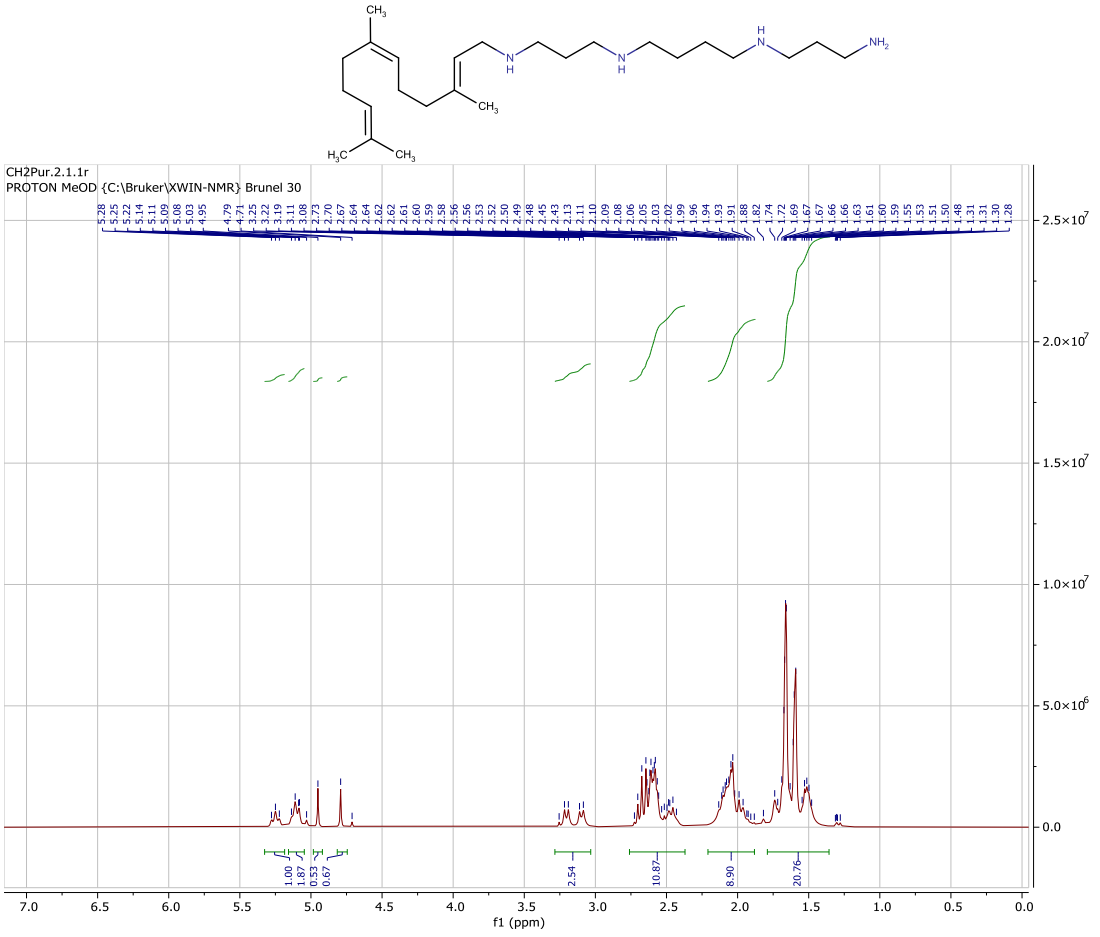
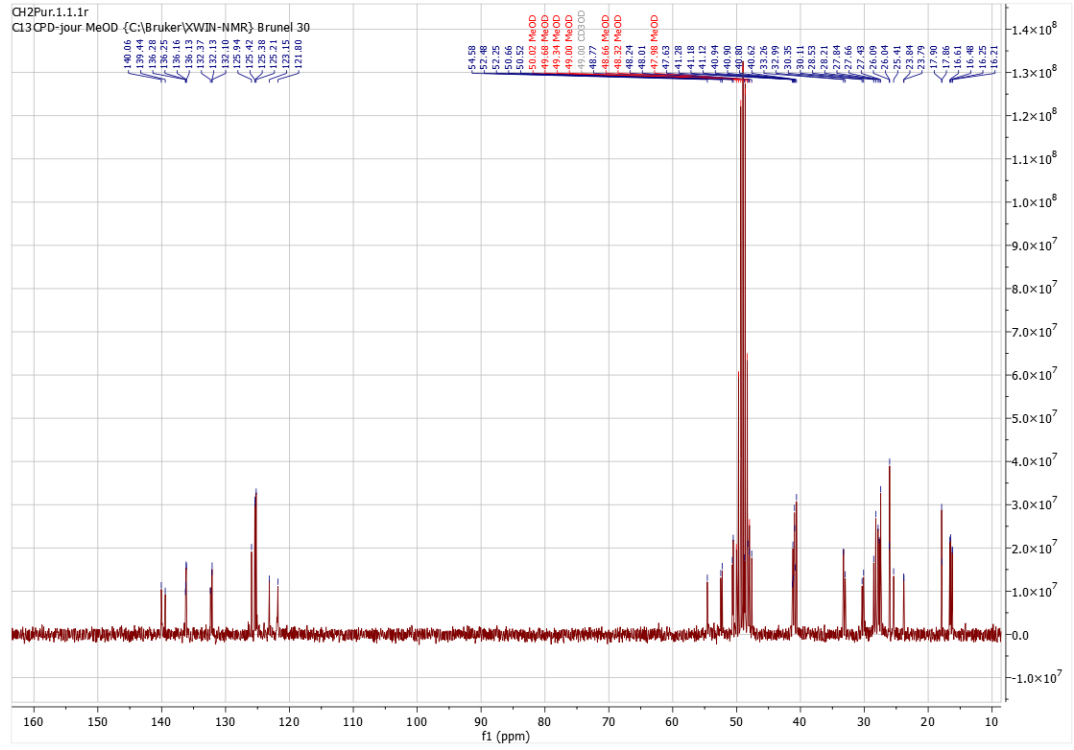
General procedure for the synthesis of polyaminoisoprenyl derivatives 3

To a solution of spermine (450 mg, 2.27 mmol) and triethylamine (450 µL, 4.5 mmol) in distillated tetrahydrofurane (THF) (10 mL) was added dropwise farnesyl chloride **1** (mixture of isomers) (480 mg, 2 mmol) in distillated THF (15 mL). The reaction mixture was stirred at room temperature for 24 h. and evaporated to dryness. The crude residue was purified by column chromatography (eluant CH_2Cl_2/MeOH/conc. NH_4OH, 7:3:1) to afford the pure desired compound as a yellow solid in 64% yield (mixture of isomers).

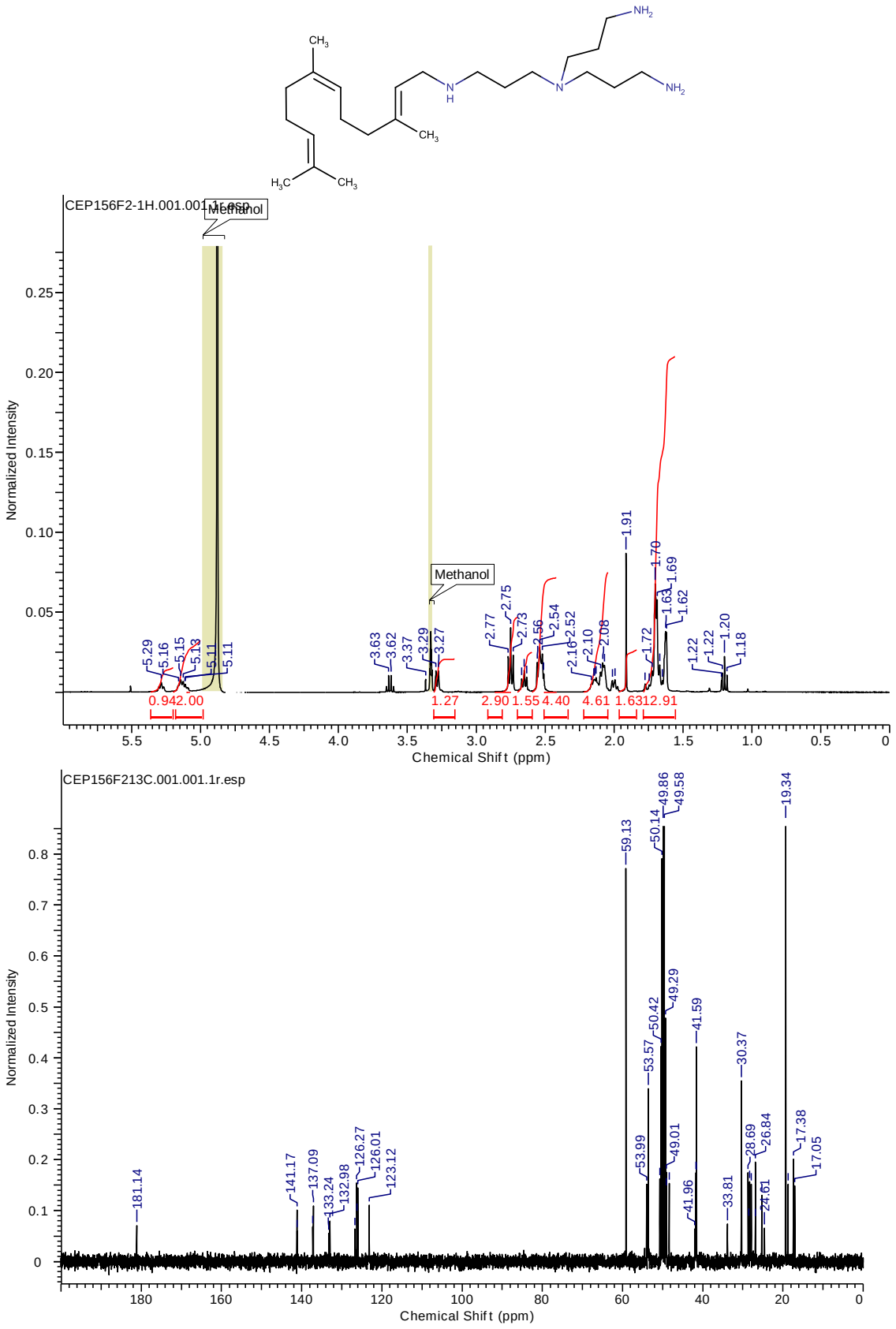
Compound 3. 64% yield; Yellow solid; ^{1}H NMR (MeOD, 250 MHz): δ = 5.22-5.25 (m, 1H), 5.03-5.14 (m, 2H), 3.11-3.25 (m, 3H), 2.50-2.73 (m, 9H), 2.43-2.49 (m, 3H), 1.96-2.11 (m, 10H), 1.69-1.74 (m, 12H), 1.50-1.67 (m, 10H). ^{13}C (MeOD): δ = 140.06, 139.44, 136.28, 136.25, 136.16, 136.13, 132.37, 132.13, 132.10, 125.94, 125.42, 125.38, 125.21, 123.15, 121.80, 54.58, 52.48, 52.25, 50.66, 50.52, 48.77, 48.24, 48.01, 47.63, 41.28, 41.18, 41.12, 40.94, 40.90, 40.80, 40.62, 33.26, 32.99, 30.35, 30.11, 28.53, 28.21, 27.84, 27.66, 27.43, 26.09, 26.04, 25.41, 23.84, 23.79, 17.90, 17.86, 16.61, 16.48, 16.25, 16.21. $C_{25}H_{50}N_4$ MS (ESI+) m/z 407.41 (100%, $[M + H]^+$).

^{1}H and ^{13}C NMR Spectra of 3

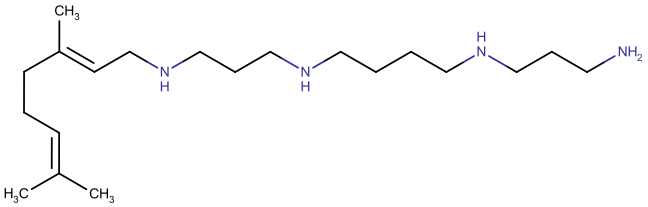


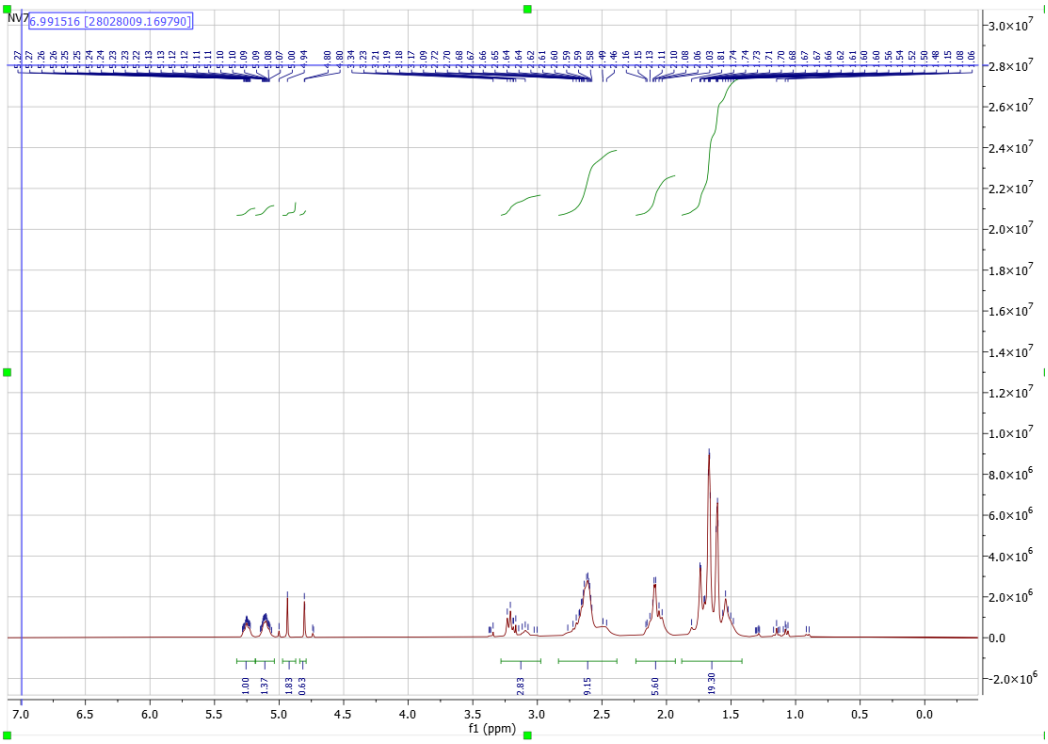


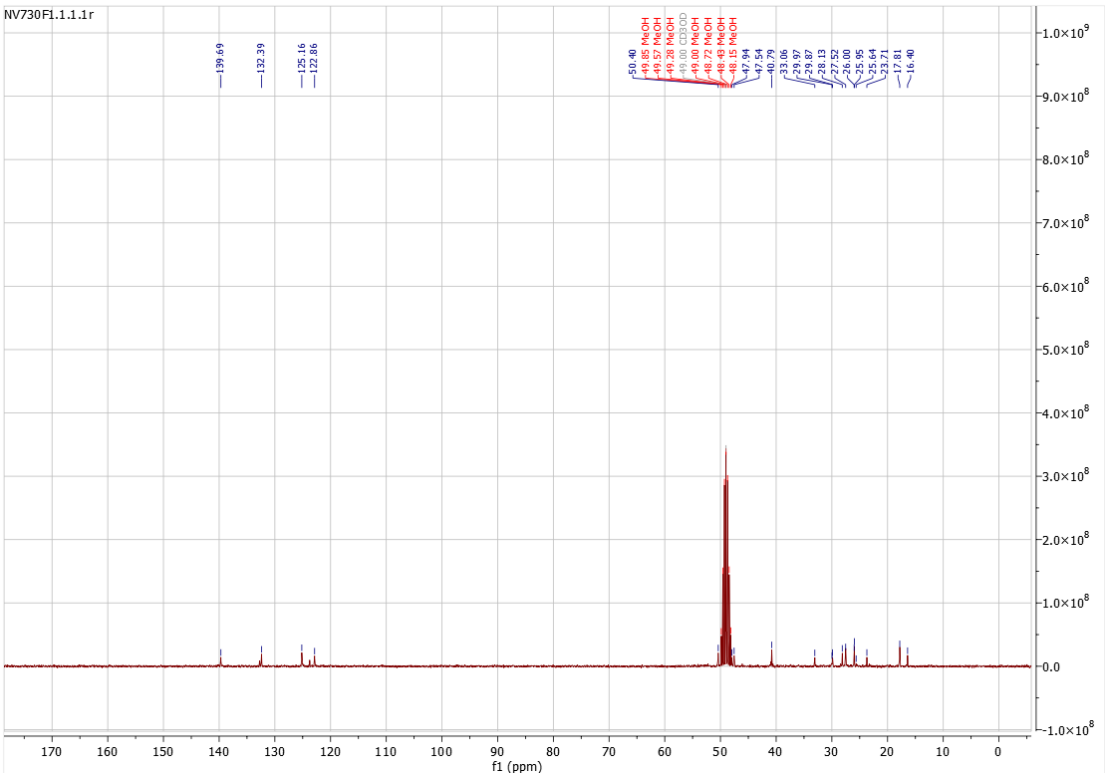
^{1}H and ^{13}C NMR Spectra of 4



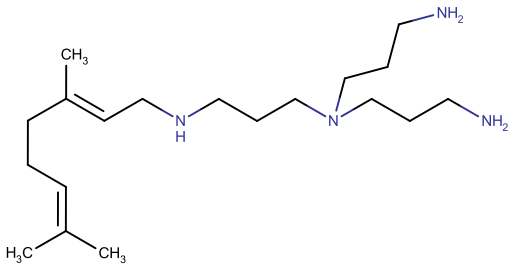
^{1}H and ^{13}C NMR Spectra of 5

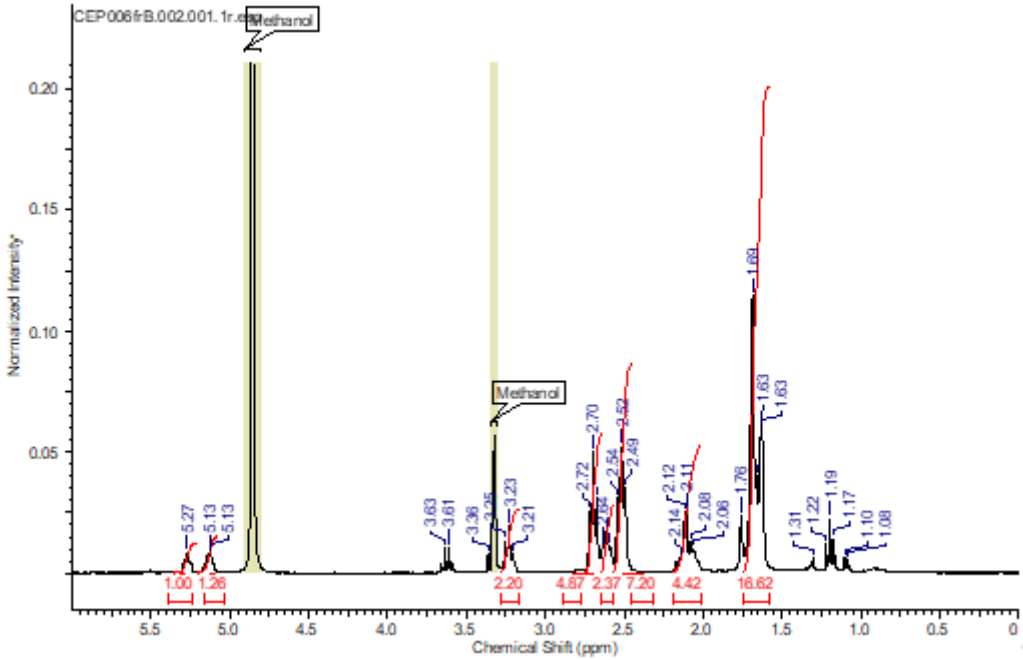






^{1}H and ^{13}C Spectra of 6





C NMR spectra of derivatives 3-6

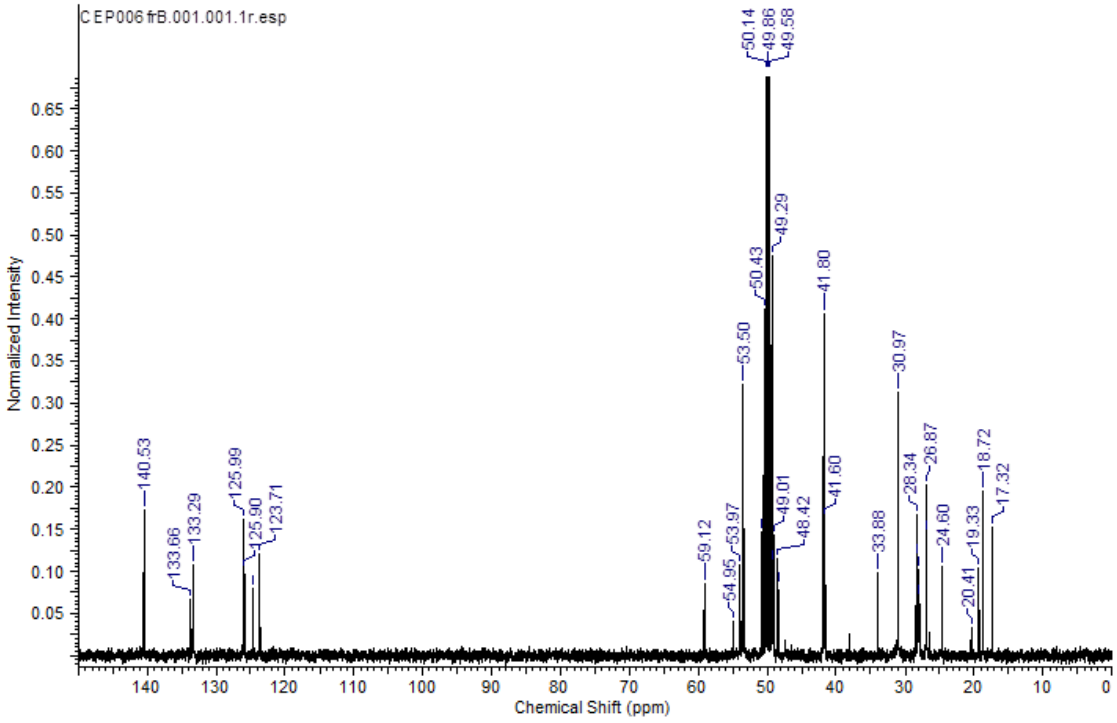


Figure S1. ^{1}H and ^{13}C NMR spectra of derivatives **3-6**

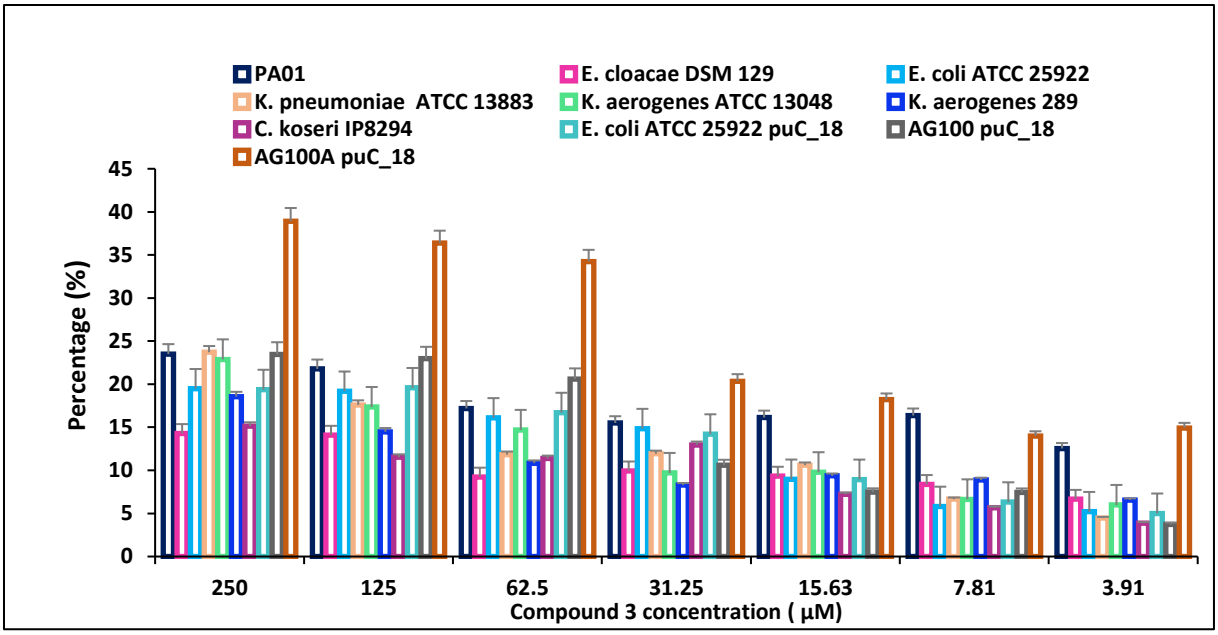


Figure S2. Dose-dependent inner membrane depolarization of various Gram-negative bacteria in the presence of compound **3**

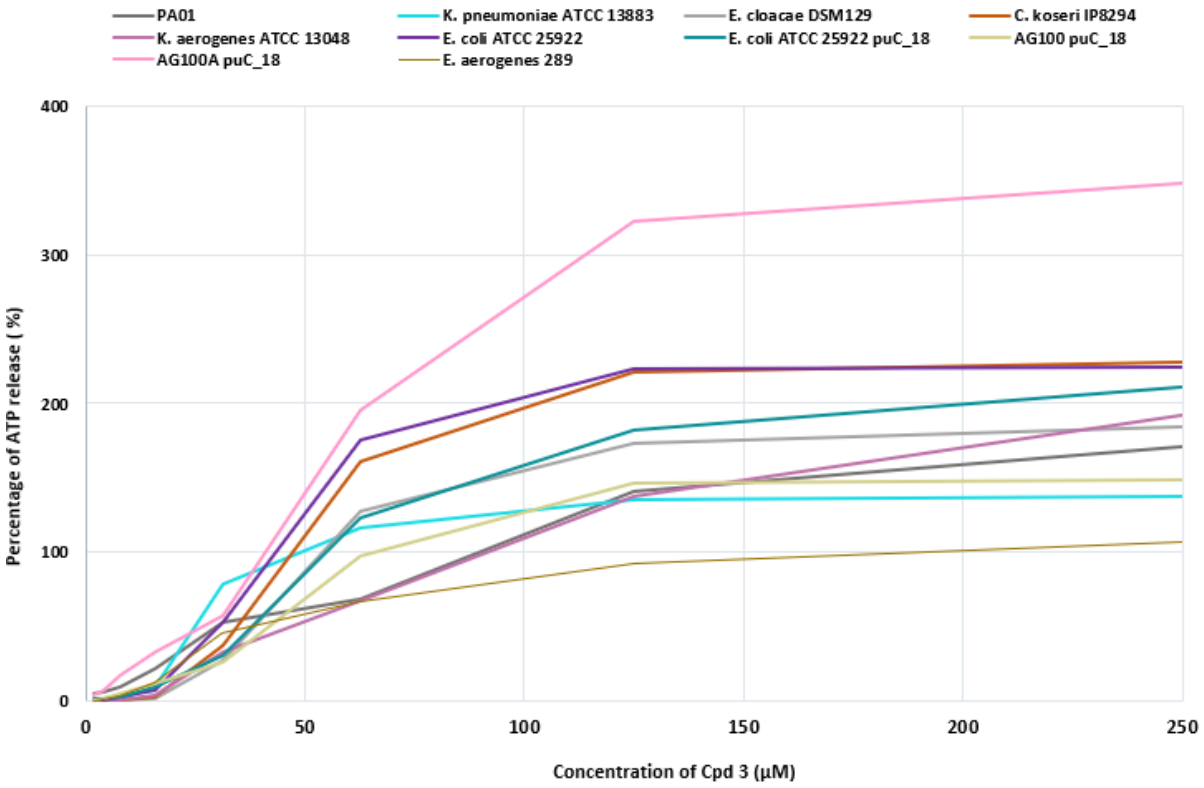


Figure S3. Dose-dependent ATP release levels of various Gram-negative bacteria evaluated by bioluminescence in the presence of compound **3**

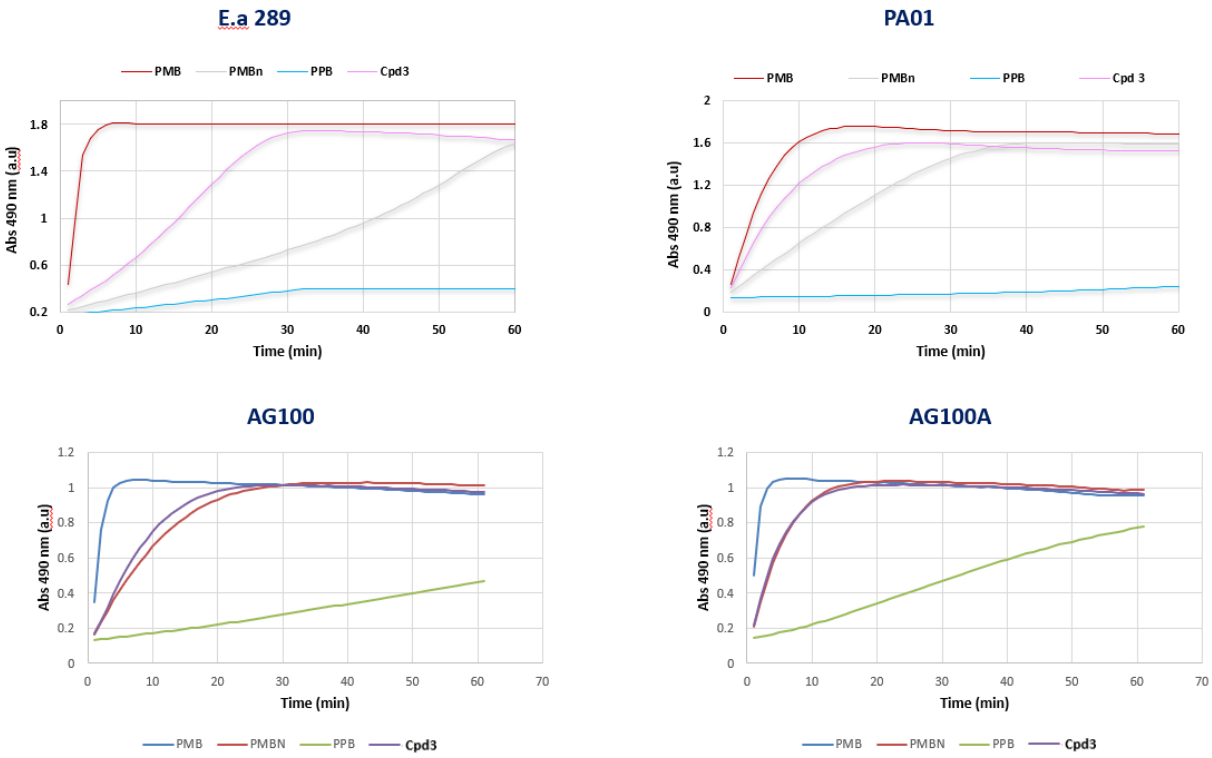


Figure S4. Comparison of the nitrocefin hydrolysis kinetics in the presence of PMB, PMBn, **3** used at a 125 µM concentration in the case Ea289, PA01, *E. coli* AG100, *E. coli* AG100A bacterial strains