As pathogenic bacterial species are becoming more resistant to commonly used antibiotics, it is essential for new antibiotics to be developed. A family of resazurin (Rz)-based compounds, resazomycins, was discovered to be highly effective antimicrobials against Neisseria gonorrhoeae (Ng) in vitro. However, when these compounds were tested in a mouse model of gonorrhea, only one resazomycin, resorufin pentyl ether (RPE), exhibited any therapeutic effect. These differences between in vitro and in vivo therapeutic efficacy may be due to differences in oxygen concentration. Most mammalian tissues exist at oxygen concentrations well below atmospheric levels, typically 2-5% instead of 20%. We hypothesized that decreased oxygen levels may confer resistance to resazomycins. To test this, we cultivated clinical isolates of Ng under different oxygen conditions and then determined the minimal inhibitory concentration (MIC) of various resazomycins. The MIC of resazurin for the different Ng isolates were up to 4-fold higher under 2% oxygen than 20% oxygen suggesting oxygen levels affect susceptibility to resazomycins. No significant difference in the MIC of RPE was observed under the different oxygen concentrations consistent with RPE being the sole resazomycin having efficacy against N. gonorrhoeae. We also calculated the MIC of three non-resazomycin based antibiotics and saw that there was no significant difference in MIC at the two oxygen concentrations. Further investigation is needed to determine how Ng is becoming resistant to resazomycins under low oxygen conditions.