Significance: Compound O is one of a series of 4-(aminomethyl)quinolin-2(1H)-ones that inhibits bacterial DNA gyrase and topoisomerase IV, and displays potent activity against ciprofloxacin-resistant Gram-negative pathogens. Unfortunately, a number of in vitro safety issues were identified that, together with severe loss of antibacterial potency at pH 5.8, led to termination of the project.

Comment: Noteworthy steps in the synthesis of O are (1) the appendage of the cyclopropyl ring to the aniline via a Chan–Lam coupling; (2) construction of the quinolin-2(1H)-one core by base-mediated Claisen condensation (H → I); appendage of the aminomethyl group via Suzuki reaction (J → L); and Buchwald–Hartwig coupling of the pyrrolidine fragment M and enol triflate J.

SYNFACTS Contributors:
Philip Kocienski

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