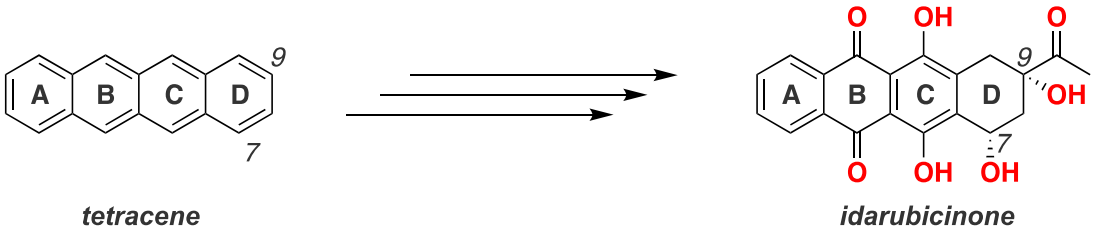
Total Synthesis of Idarubicinone

David Dennis and David Sarlah

A concise synthesis of the aglycone anthracycline idarubicinone from tetracene has been accomplished. Direct oxidation of tetracene circumvents the need for traditionally-required annulation strategies for the construction of the tetracyclic core while providing the desired oxidation states of the A–C rings. A dearomative hydroboration provides direct access to the requisite C-9 functionality *via* olefination. Finally, three net redox-neutral transformations of the dearomatized D-ring sequentially install the desired hydroxyl functionality to afford idarubicinone in nine steps from tetracene.

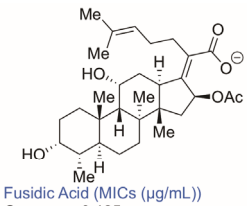


tetracene *idarubicinone*

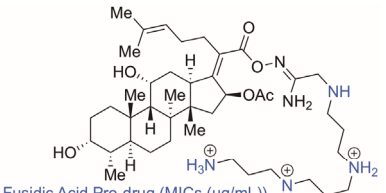
Development of Broad-spectrum Antibiotics via Rational Design

Martin Garcia Chavez, Alfredo Garcia, and Paul J. Hergenrother

Multi-drug resistant bacteria are a major threat to human health worldwide. Even more concerning is the appearance of Gram-negative bacteria in the clinic that are insensitive to all antibiotic classes. Exacerbating this issue is the fact that a new class of antibiotics with efficacy against Gram-negative bacteria has been not been introduced to the clinic since the quinolones in the 1960s. As a result, novel classes of broad-spectrum antibiotics that can combat these deadly pathogens are urgently needed. Fusidic acid, a potent Gram-positive-only antibiotic was chosen as a conversion target due to its valuable translational potential. The development of a novel pro-drug approach generated the first fusidic acid derivative with potent activity in Gram-negative bacteria. Future work will include assessing the generality of this new conversion paradigm with other FDA approved antibiotics.



Fusidic Acid (MICs (μg/mL))
S. aureus: 0.125
E. coli: 512
A. baumannii: 64
K. pneumoniae: 1024
E. cloacae: 512
P. aeruginosa: 1024



Fusidic Acid Pro-drug (MICs (μg/mL))
S. aureus: 1
E. coli: 4
A. baumannii: 2
K. pneumoniae: 16
E. cloacae: 8
P. aeruginosa: 4

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