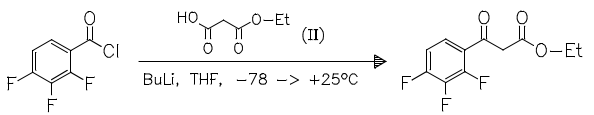
Oxazine derivatives

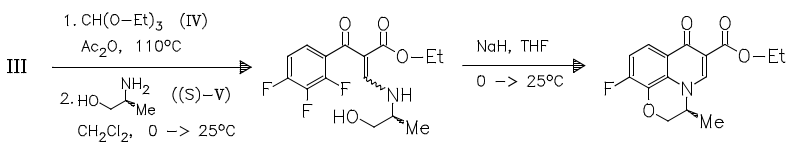
R 0595

42- 162

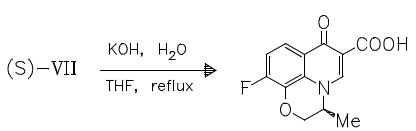
Synthesis and Biological Testing of Non-Fluorinated Analogues of Levofloxacin. — The non-fluorinated Levofloxacin analogues are prepared following an earlier report on the synthesis of the 6F quinolone nucleus. The closure of the N-1 to C-8 ring for benzoxazine formation is best effected by continued treatment with base [(VI) → (VII)] in the quinolone ring formation step rather than with KOH in the ester hydrolysis step. The new pyrrolidine containing quinolones (X) maintain good antibacterial potency relative to the parent molecule while the piperidine and piperazine containing quinolones show dramatically reduced potency. — (GRAY*, J. L.; ALMSTEAD, J.-I. K.; GALLAGHER, C. P.; HU, X. E.; KIM, N. K.; TAYLOR, C. J.; TWINEM, T. L.; WALLACE, C. D.; LEDOUSSAL, B.; Bioorg. Med. Chem. Lett. 13 (2003) 14, 2373-2375; Procter & Gamble Pharm., Mason, OH 45040, USA; Eng.) — H. Hoennerscheid



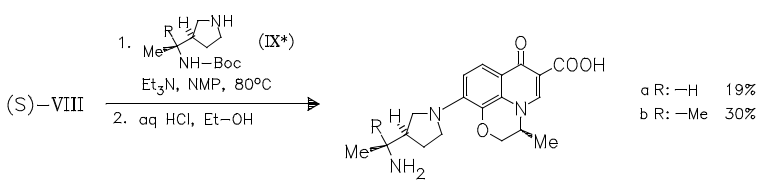
I III 65%



(S)−VI 78% (S)−VII 73%



(S)−VIII 89%



X*