ABSTRACT SAMPLE

Restricted to one page

170 mm or $6^{3/4}$ inches

235 mm or $9^{1/4}$ inches

(Abstract Title)

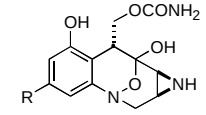
Asymmetric Synthesis of FR900482

(Author's List and Institutional Address)

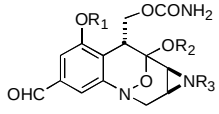
Ted Judd and Robert M. Williams*
Department of Chemistry, Colorado State University
Fort Collins, Colorado 80523

(Abstract Text & Graphics)

The antitumor antibiotic natural products FR900482 (**1**) and FR66979 (**2**) were isolated from *Streptomyces sandaensis* No. 6897 by the Fujisawa Pharmaceutical Co. in 1987. Recent studies from our laboratory have demonstrated that FR900482 (**1**) and FK317 (**4**) cross-link the minor groove-binding HMGA1 oncoprotein to DNA *in vivo*, which has very significant implications for the mode of action of these agents. Both FK973 (**3**) and FK317 (**4**), semi-synthetic derivatives of FR900482 (**1**), have shown highly promising antitumor activity in human clinical trials in Japan

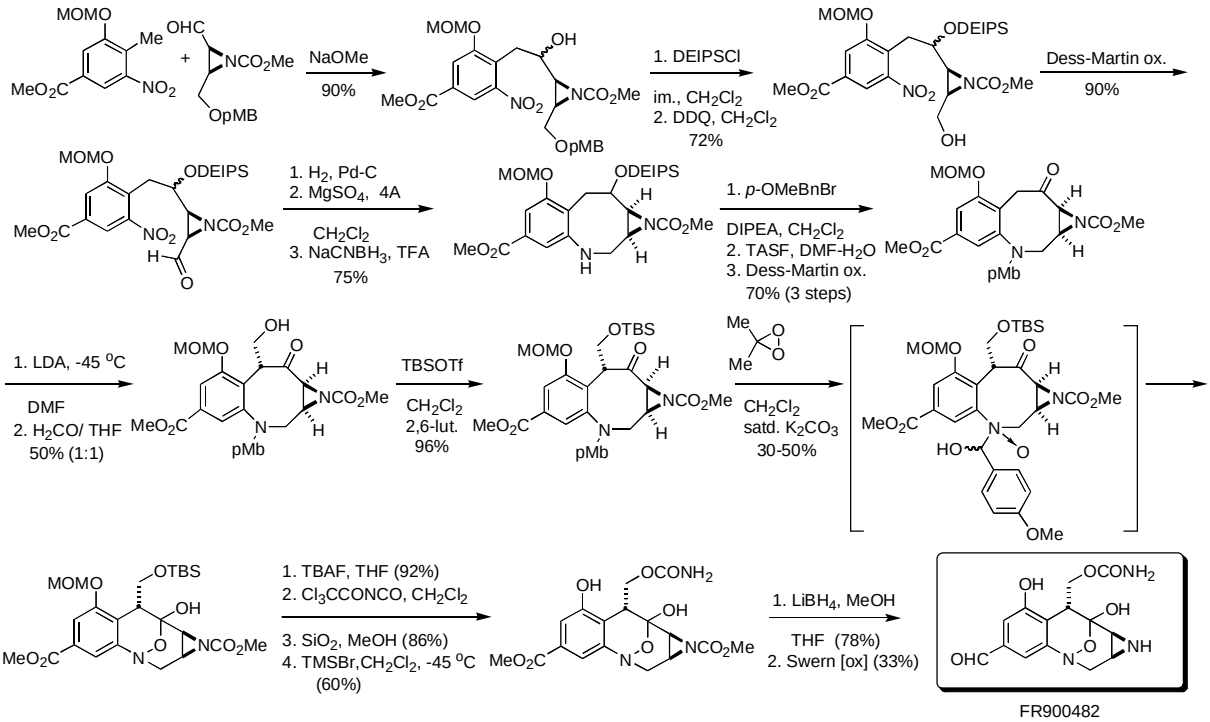


1, FR-900482, R = CHO
2, FR-66979, R = CH_2OH



3, FK-973, R_1= R_2 = R_3 = Ac
4, FK-317, R_1 = Me, R_2 = R_3 = Ac

Dimethyldioxirane effects the remarkable one-step deprotection/oxidative cyclization of an eight-membered ring amino-ketone to the unique hydroxylamine hemi-ketal ring system of FR900482, a clinically significant antitumor antibiotic. This reaction has been exploited in a concise thirty-three step enantioselective total synthesis of FR900482, which constitutes the shortest synthesis of this natural product reported to date.



FR900482

Williams, R.M.; Rollins, S.B.; Judd, T.C., *Tetrahedron*, **2000**, *56*, 521~532.
Judd, T.; Williams, R.M., *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 4683~4685.
Judd, T.; Williams, R.M., *Org. Lett.* **2002**, *4*, 3711~3714.