ring closure reactions

O 0130

10 - 048

The Preparation and Intra- and Intermolecular Addition Reactions of Acyclic N-Acylimines: Application to the Synthesis of (±)-Sertraline. — Careful reduction of imides of type (I) generates remarkably stable acyclic hemiacetals [cf. (II)] which undergo intramolecular nucleophilic addition to give various cyclized products. The methodology is applied to the synthesis of racemic sertraline (XVIII). The intermolecular variant affords products of type (XIV). — (DENINNO, MICHAEL; ELLER, CYNTHIA; ETIENNE, JOHN B.; J. Org. Chem. 66 (2001) 21, 6988-6993; Pfizer Global Res. Dev., Pfizer Inc., Groton, CT 06340, USA; EN)
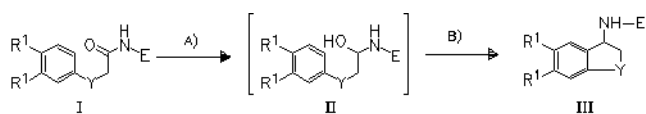
a R¹: —H ; Y: —CH₂— ; E: —Moc   a 0%
b R¹: —H ; Y: —(CH₂)₃— ; E: —Cob   b 39%
c R¹: —O—Me ; Y: —(CH₂)₂— ; E: —Moc   c 79%

Moc: —CO—O—Me   Cob: —CO—O—Bn

A): iBu₂AlH, CH₂Cl₂, toluene, −78°C, [1.5 h]   B): 1.5 equiv. TiCl₄, CH₂Cl₂, −78°C

C): 1.5 equiv. BF₃·OEt₂, CH₂Cl₂, −60°C

a E: —Moc   76% (1:1 m.d.)
b E: —Cob   80% (1:1 m.d.)

a R: 65% (0% d.e.)
b R: 73% (25% d.e.)
c R: 70% (40% d.e.)

a R²: —CH₂ ; X: —SiMe₃ ; Z: —CH₂—   80%
b R²: ; X: —H ; Z: —(CH₂)₂—   68%
c R²: ; X: —H ; Z: —(CH₂)₂—   78%

Dcp:

2