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Stereoselective Total Synthesis of (–)-Flueggine A and (+)-Virosaine B  $\,$ 

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## Total Synthesis of (–)-Flueggine A and (+)-Virosaine B

A steps

A steps

A steps

A steps

D (5 mol%) 64% relay ring-closing metathesis

D (5 mol%) 64% phMe, 
$$\Delta$$

G (-)-Norsecurinine (E)

Xylene,  $\Delta$ 
85% Meisenheimer rearrangement

(2 steps)

H MCPBA

MCPBA

A steps

D (5 mol%) 67% phMe,  $\Delta$ 
(-)-Allonorsecurinine (F)

Xylene,  $\Delta$ 
85% (2 steps)

H MCPBA

MCPBA

A steps

A steps

D (5 mol%) 67% phMe,  $\Delta$ 
(-)-Allonorsecurinine (F)

Xylene,  $\Delta$ 
82% (2 steps)

A steps

H MCPBA

H MCPBA

A steps

A s

Significance: Securinega alkaloids have been used for a long time in traditional Chinese medicine. Two recently isolated members of this family, (–)-flueggine A and (+)-virosaine B, have now been synthesized for the first time. The concise route to access the two natural products involves a [1,3]-dipolar cycloaddition. The precursors for this key step are synthesized by a sequence including a relay ring-closing metathesis followed by a Meisenheimer rearrangement.

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Comment: The route starts with the synthesis of the two natural products (–)-norsecurinine (**E**) and (+)-allonorsecurinine (**F**) by a relay ring-closing metathesis, whereby the order of ring-closing events can be carefully controlled. The route then follows a previously described strategy (*Tetrahedron* 1993, 49, 8059) to access the two *O*-alkylhydroxylamines **H** and **K**. Finally, heterodimeric (–)-flueggine A is accessed by allowing nitrone **I** to react with **E**, whereas (+)-virosaine B results from an intramolecular cycloadditon of nitrone **L**.

Category

Synthesis of Natural Products and Potential Drugs

**Key words** 

dipolar cycloaddition

relay ring-closing metathesis

[1,3]-sigmatropic rearrangement

Meisenheimer rearrangement



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