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Studies toward total synthesis of natural products of Miliusanes family

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Introduction

Miliusane monomers and the associated dimers are cytotoxic compounds isolated from Miliusa sinensis Finet and Gagnep.[1] Recent studies have shown that they have anti-inflammatory, antitumor, and antifibrotic activities.[2] Structurally, they are a cluster of compounds composed of a C-18 carbon skeleton including two substructural classes, One possesses a γ-lactone spiro-ring system and the other contains a tetrahydrofuran ring system. The synthesis of such molecules is extremely challenging because the whole molecule is spatially crowded due to the chiral center of the quaternary carbon and the chirality of the side chains. Our effort is concerned on the study of the total synthesis of this family of natural products.

Miliusanes Family

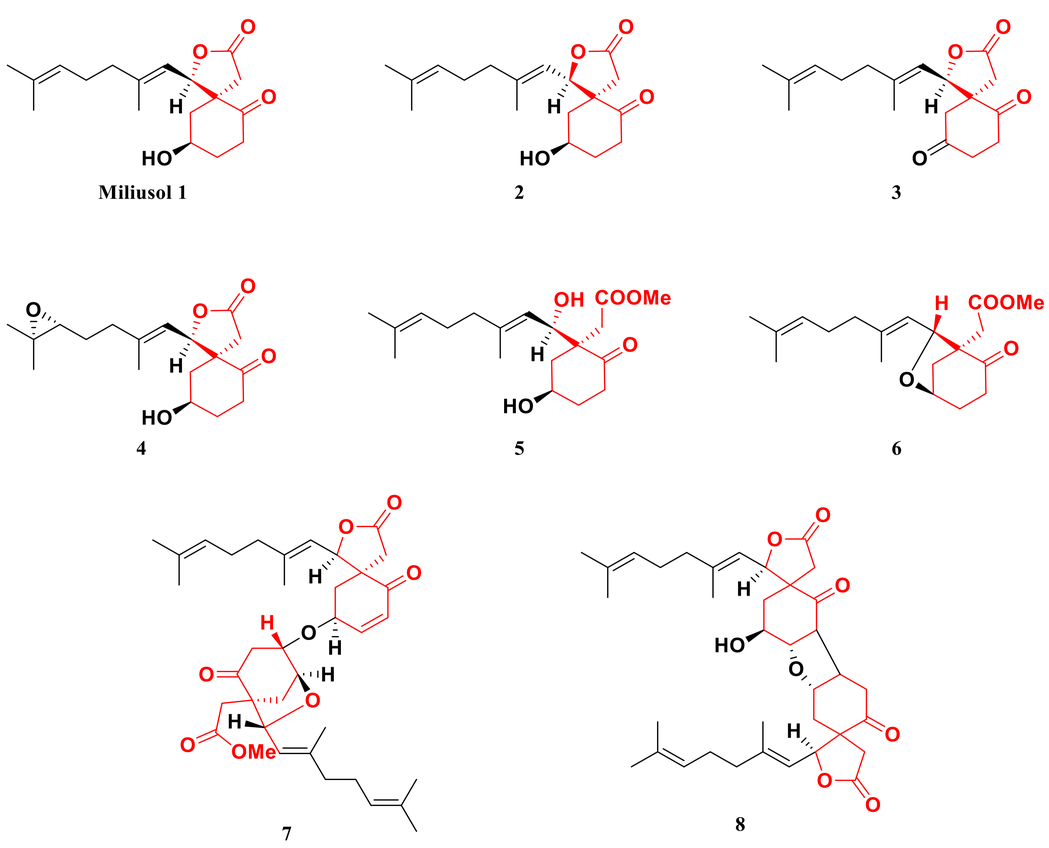


Figure 1. Examples of miliusane and dimer

Construction of chiral center of quaternary carbon

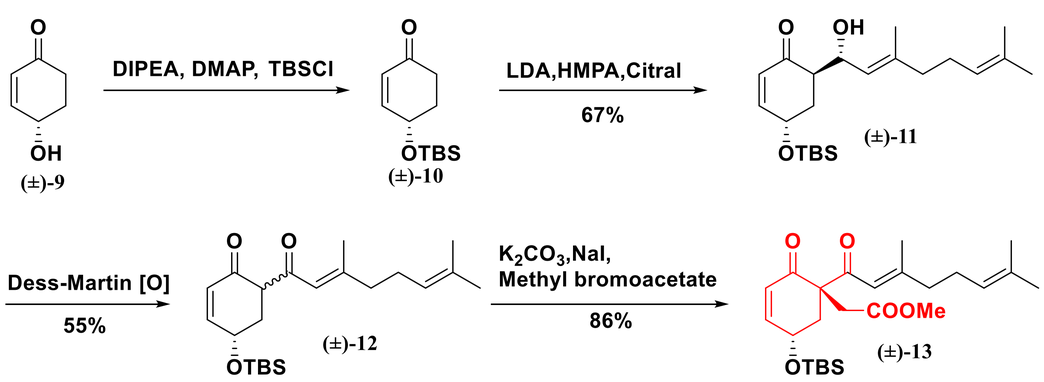
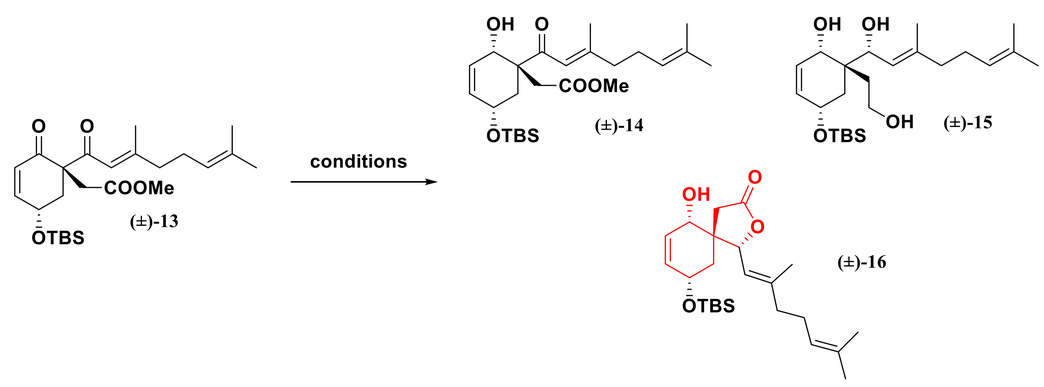


Figure 2. Synthesis of (±)-13

Construction of spiro-ring

Table 1. Selective reduction of carbonyl groups



entry	condition	products (yield,%)
1	DIBAL-H (4 eq.), -78℃	NR
2	DIBAL-H (4 eq.), rt	Mixture
3	LiAlH(Ot-Bu)3 (4 eq.), -78℃	NR
4	LAH (3 eq.), 0℃	Mixture
5	NaBH4 (3 eq.), CeCl3·H2O (1.1 eq.)	(±)-14 (58), (±)-16 (29)

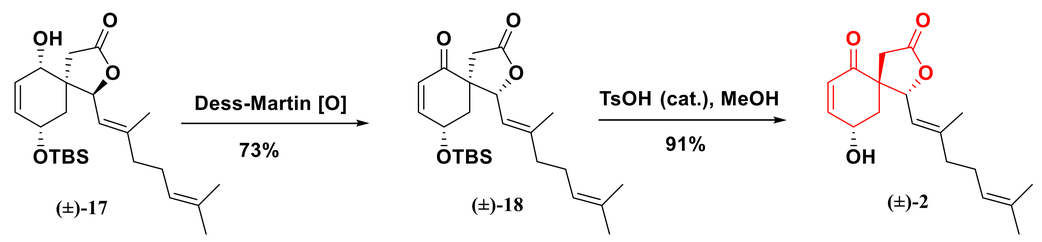


Figure 3. Construction of epimer (±)-2

Reference

1. (a) Wu, R.; Ye, Q.; Chen, N. Y.; Zhang, G. L. *Chin. Chem. Lett.* **2001**, *12*, 247- 248.
(b) Huong, D. T.; Kamperdick, C.; Sung, T. V. *J. Nat. Prod.* **2004**, *67*, 445-447.
2. Hong-Jie Zhang.;Cuiying Ma.; Nguyen Van Hung.; Nguyen Manh Cuong.; Ghee Teng Tan.; Bernard D. Santarsiero.; Andrew D. Mesecar.; D. Doel Soejarto.; John M. Pezzuto.; Harry H. S. Fong. *J.Med.Chem.* **2006**, *49*, 693-708.

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