

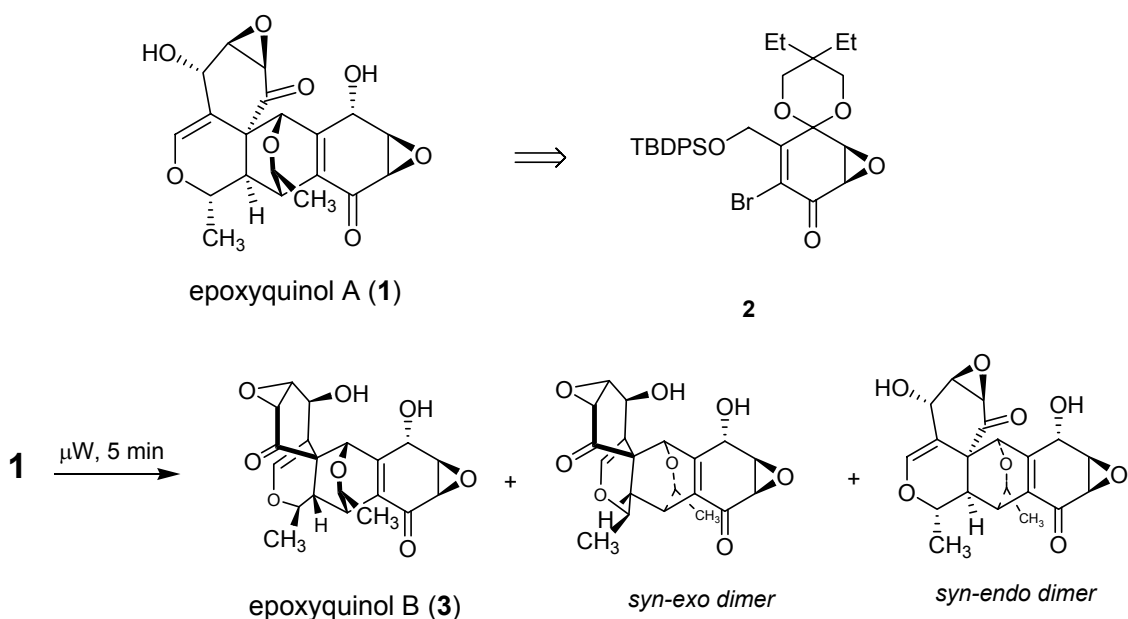


## The Angiogenesis Inhibitor Epoxyquinol A: Total Synthesis and Inhibition of Transcription Factor NF- $\kappa$ B:

Angiogenesis, new blood vessel formation, involves a number of distinct processes, including endothelial cell migration, proliferation, and capillary tube formation, and is believed to be a key requirement for tumor growth and metastasis. The pentaketide dimer (+)-epoxyquinol A (**1**) (Figure 1) was recently isolated from an uncharacterized fungus by Osada and coworkers and was shown to have potent antiangiogenic activity.

Recently, we achieved the first total synthesis and absolute stereochemical assignment of this interesting natural product. The synthesis utilized a known intermediate **2** from our synthesis of cycloepoxydon and was accomplished in five steps (32.6% overall yield). In addition, one epoxyquinone dimer and three epoxyquinol dimers were also synthesized, one of which was later proved to be another natural product epoxyquinol B (**3**). Notably, two of these epoxyquinol dimers were generated using microwave irradiation.

Figure 1



Further biological experiments showed dimeric epoxyquinol A and B (**1** and **3** above) and two monomeric synthetic intermediates all inhibit tumor necrosis factor (TNF)-induced activation of NF- $\kappa$ B DNA binding in mouse 3T3 cells. *Org. Lett.* **2002**, *4*, 3267-3270.