

Synthesis and Biological Evaluation of a Series of Aromatic Bisphosphonates.

Geminal bisphosphonates display varied biological activity depending in the nature of the substituents on the central carbon atom. For example, the nitrogenous bisphosphonates zoledronate and risedronate inhibit the enzyme farnesyl diphosphate synthase while digeranyl bisphosphonate has been shown to inhibit the enzyme geranylgeranyl diphosphate synthase. We now have synthesized isoprenoid olefins in an isoprenoid bisphosphonate and investigated the ability of these new compounds to impair protein geranylgeranylation within cells. Several of these new compounds are potent inhibitors of the enzyme geranylgeranyl diphosphate synthase.