

STEREOSPECIFIC TOTAL SYNTHESIS OF dl-TAONDIOL METHYL ETHER

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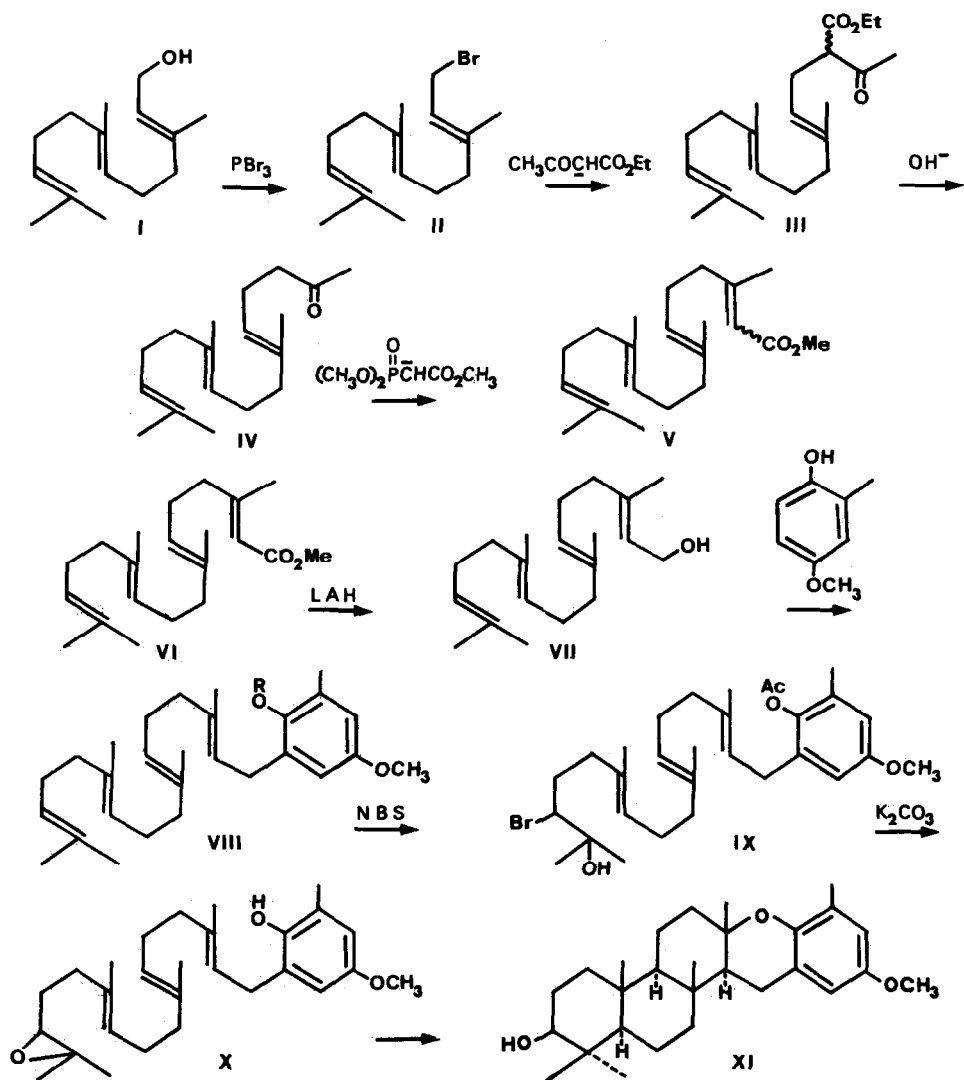
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Many examples of stereoselective synthesis of polycyclic fused-ring compounds by nonenzymic, cationic cyclization of polyolefins are known<sup>1</sup>. The impressive work undertaken at Stanford<sup>2,3</sup> and Harvard<sup>4</sup> has reduced to laboratory practice certain aspects of the stereospecific synthesis and cyclization of polyenes.

We wish to report the total synthesis of dl-taondiol methyl ether (XI)<sup>5</sup>, featuring the stereoselective generation of six asymmetric centers during cyclization of epoxide X. The synthetic sequence leading from trans,trans-farnesol (I) to the desired prenyl phenol terminal epoxide X involved nine steps, and is outlined in Scheme 1.

trans,trans,trans-Geranylgeraniol (VII) was obtained from I by modification of the Ruzicka procedure<sup>6</sup>. Following a general method for the modification of the Wittig reaction described by Wadsworth and Emmons<sup>7</sup>, farnesylacetone (IV) was converted to a mixture of methyl geranylgeranate (V, 65:35 trans, cis  $\alpha,\beta$ -unsaturated ester mixture). After purification of the all-trans-isomer VI by chromatographic means, geranylgeraniol was prepared by lithium aluminum hydride reduction.

Condensation of VII with toluquinol 4-methyl ether<sup>8</sup> at r.t. in dry dioxane with the aid of boron trifluoride<sup>5</sup> afforded a mixture of products from which, after chromatographic purification on silica gel, the desired compound



SCHEME 1

VIII (R=H) was isolated in 54% yield [acetate VIII (R=Ac), pmr ( $\text{CCl}_4$ ,  $\tau$ -scale): 3.18 (2H,s); 4.90 (4H,m); 6.21 (3H,s); 6.61 (2H,d,J=8 Hz); 7.80, 7.95, 8.24, and 8.35 (each 3H,s); and 8.43 (9H,s)]. N-Bromosuccinimide oxidation of the acetate VIII (R=Ac) in aqueous tetrahydrofuran<sup>9</sup> provided the terminal bromohydrin IX, which on treatment with potassium carbonate in methanol gave the terminal epoxide of the free alcohol X [pmr: 3.41 (2H,s); 3.95 (1H,s); 4.60-5.05 (3H,m); 6.35 (3H,s); 6.74 (2H,d,J=8 Hz); 7.30 (1H,t,J=6 Hz); 7.90, and 8.31 (each 3H,s); 8.40, and 8.76 (each 6H,s)].

Treatment of X with 0.2 molar equiv of stannic chloride in benzene for 5 min at 10-15° gave, in 35% yield, the crystalline compound XI, m.p. 201-203°. Its pmr spectrum shows two meta-coupled protons at 3.47 and 3.57 (2d,1H each, J=2.5 Hz), one three-protons singlet at 6.28 (OMe), a broad signal at 6.77 (1H,m,W/2=14 Hz, H-C-OH), two benzyl protons at 7.39 (d,broad,J=8 Hz), one aromatic Me group at 7.88 (3H,s), and a singlet at 8.86 (3H, Me-C-O-). Signals for four tertiary methyl groups appear at 9.01, 9.11, 9.13, and 9.19 (each 3H,s). By direct comparison with an authentic sample, compound XI was shown to be identical with teondiol methyl ether<sup>5</sup>.

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