Total Synthesis of (±)-Jolkinolide A and B

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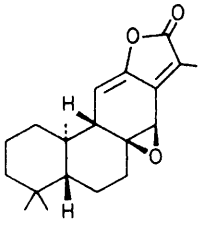
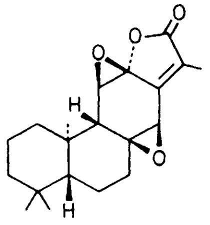
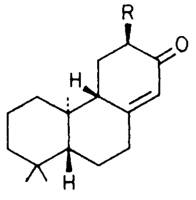
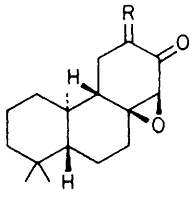
The first efficient synthesis of jolkinolide A and B from the diosphenol (**7**) is reported; the new synthetic method described may find use in the preparations of 4-ylidene-2,3-substituted butenolides.

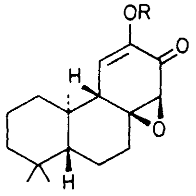
Previously we reported an efficient synthesis of jolkinolide E from the α-hydroxyenone (**4**) ester of α-(diethylphosphono)-propionic acid by intramolecular Wittig reaction. In that synthesis we developed a facile esterification method involving a mixed anhydride of trichloroacetic acid and catalysed by 4-dimethylaminopyridine.[1] We have now extended this procedure to a synthesis of the more complex butenolide, jolkinolide A (**1**) which may be converted into jolkinolide B (**2**) isola-

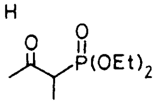

jolkinolide A (**1**)

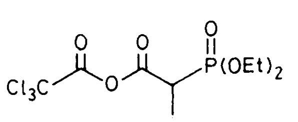

jolkinolide B (**2**)


(**3**) R = H
(**4**) R = OH


(**5**) R = H, H
(**6**) R = CHNMe$_2$


(**7**) R = H

(**8**) R =



(**9**)

ted from *Euphorbia Jolkini Boiss.*[2] Jolkinolide B has a novel epoxylactone function and its growth inhibition to cultured Hella Cell has been reported.

Our key intermediate, diosphenol (**7**), was prepared from epoxyketone (**5**), m.p. 98—99 °C, derived from tricyclic enone (**3**)[1] (H_2O_2, OH^-, quantitatively) by Wasserman's method.[3] Enaminoketone (**6**), m.p. 133.5—135 °C, obtained from (**5**) with t-butoxybis(dimethylamino)methane (neat, 60—65 °C, overnight, 87% yield) was oxygenated (O_2, catalytic amount of tetraphenylporphine, CH_2Cl_2, −78 °C, 300 W iodohalogen lamp) to give (**7**),† m.p. 185—186 °C, in 60% yield. The mixed anhydride (**9**), generated from α-(diethylphosphono)propionic acid with trichloroacetyl chloride in the presence of triethylamine (tetrahydrofuran, room temp.), was allowed to react with (**7**) with the aid of 4-dimethylaminopyridine yielding (**8**) which was used without purification in the next step (after working up) because it gradually hydrolysed to (**7**) during SiO_2 chromatography. The final step was a clean intramolecular Wittig reaction. The synthesis of jolkinolide A [in 82% yield based on (**7**)] was completed by treatment of crude (**8**) with NaH (1.2 equiv., 1,2-dimethoxyethane, room temp., 5 min.). The jolkinolide A obtained, m.p. 202—203 °C, was converted into jolkinolide B (**2**), m.p. 221—222 °C, with the aid of *m*-chloroperbenzoic acid[2] and both compounds were identical with the natural compounds (i.r., ^{1}H n.m.r., u.v., and mass spectra). The intramolecular Wittig reaction above promises to be useful in the synthesis of 4-ylidene-2,3-substituted butenolides.[4]

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† The ^{1}H n.m.r. spectrum of (**7**) in $CDCl_3$ showed that 70% of (**7**) existed as the diosphenol.