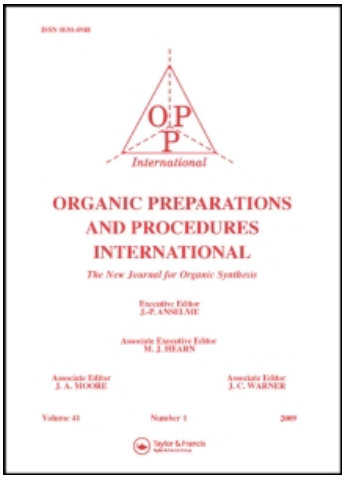

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A ONE-STEP SYNTHESIS OF OCIMIN BY A *bis*-WITTIG REACTION

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A ONE-STEP SYNTHESIS OF OCIMIN BY A bis-WITTIG REACTION

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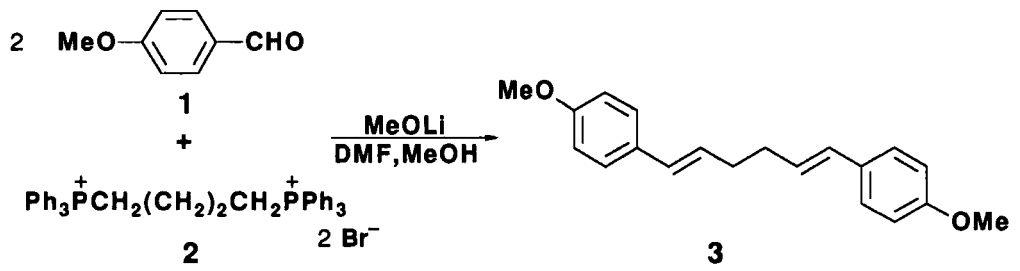
Ocimin (3), a neolignan isolated[1] from Ocimum americanum L. has been synthesized earlier by us[2] as well as by Stevenson and Ganeshpure[3] by multi-step sequences. We now report a one-step synthesis of ocimin (3) by the Wittig[4] reaction of p-anisaldehyde (1) with 1,4-bis(triphenylphosphonium)butane dibromide (2) using lithium methoxide in DMF-MeOH. The ylide, with 1,4-bis(triphenylphosphoranylidene)butane, derived from 2 using lithium methoxide reacts with p-methyoxybenzaldehyde to give ocimin (3) in one step.



EXPERIMENTAL SECTION

The NMR was recorded on Varian XL-100 and IR on Perkin-Elmer-783 instrument. The mp. is uncorrected. The silica gel used was BDH 60-120 mesh.

Ocimin (3).- To a vigorously stirred and heated (90°) solution of p-anisaldehyde (2.72 g) and 1,4-bis(triphenylphosphonium)butane dibromide[5] (8.2 g) in dry DMF (150 ml) was added lithium methoxide in methanol (prepared from 280 mg of lithium and 35 ml of dry methanol) over 3 hrs under a nitrogen atmosphere. The solution was stirred at 90° for a further period of 1 hr and most of the solvent was removed in vacuo. Water (50 ml) was added and the material extracted with ethyl acetate. The ethyl acetate was washed with water and dried over anhydrous sodium sulfate. The product obtained after removal of solvent was chromatographed over silica gel (70:30 pet ether-chloroform) to give 1.2 g (41%) of pure ocimin as fluorescent flakes, mp. 169-170° (ethyl acetate), lit.[1] mp. 170-171°. The IR and PMR spectra agreed with the reported data.[1,2] ^{1}H NMR (100 MHz, $CDCl_3$): δ 2.35 (4H, broad triplet, J = 3 Hz, allylic methylene), 3.8 (6H, s, 2 OMe), 5.9-6.3 (2H, complex multiplet, olefinic protons β to ring), 6.4 (2H, d, J = 16 Hz, olefinic protons α to ring), 6.82 (4H, d, J = 8 Hz, ArH ortho to OMe) and 7.27 (4H, d, J = 8 Hz, ArH meta to OMe).

Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.6; H, 7.5. Found: C, 81.7; H, 7.4

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A DIRECT APPROACH TOWARD THE SYNTHESIS OF ANALOGS OF ERBSTATIN

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Tyrosine-specific protein kinases (TPK) constitute an important family of phosphoryl transfer enzymes which are critical to normal cellular growth and differentiation.[1] Aberrant expression of certain TPK's has been associated with a number of neoplastic diseases including skin, breast, renal, prostate and colon cancers. Currently TPK's are the object of intense study directed toward elucidation of their function and relationship to oncogenic states. Since its isolation by Umezawa in 1986,[2] the TPK-specific inhibitor erbstatin **4c** has proven to be a useful tool in these studies and has become a widely used standard of kinase inhibition.

To date seven syntheses of erbstatin have been described.[3] Six of these procedures,[4-9] while achieving satisfactory yields, require four or more steps each. The seventh procedure, which provided a very efficient two step synthesis of erbstatin,[10] utilized the reaction of