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ENOL ETHERS : PREPARATION AND SYNTHETIC APPLICATIONS

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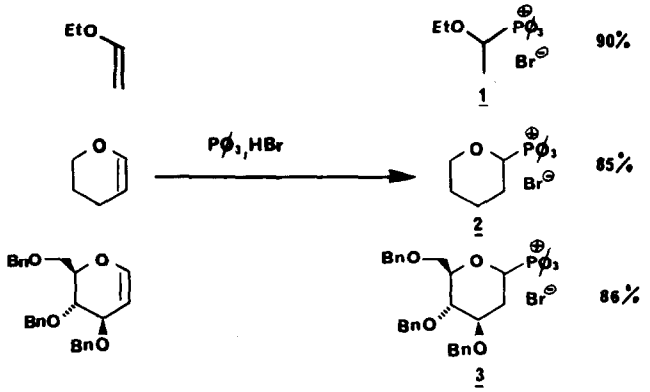
Summary : A versatile preparation of α-alkoxyphosphonium bromides leading to enol ethers by Wittig coupling was exploited for the convergent synthesis of pheromones from the Douglas-fir tussock moth and the olive fly Dacus oleae as well as an oxaspirolactone and C-glycoside.

Wittig-type olefinations[1-4] have been widely used for the preparation of enol ethers whose high reactivity and unique chemistry makes them attractive synthetic intermediates[5]. The scope of this approach, however, is trammeled in many instances by the limited availability of suitably functionalized Wittig reagents. We describe herein a versatile preparation of α-alkoxyphosphonium bromides leading to enol ethers by Wittig coupling[6] and their strategic utility in the convergent synthesis of pheromones from the Douglas-fir tussock moth and the olive fly Dacus oleae as well as an oxaspirolactone and C-glycoside.

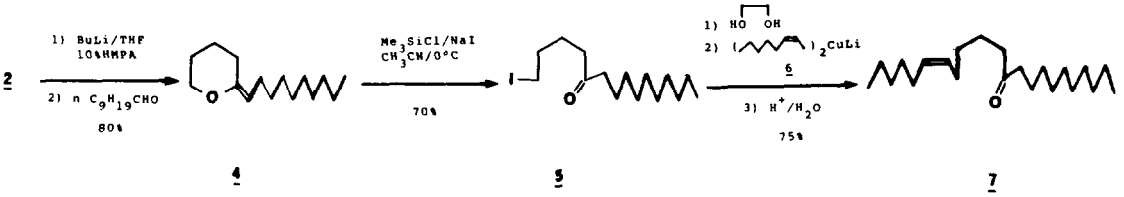
Phosphonium bromides 1-3 were readily prepared by addition of the appropriate enol ether to a 0°C solution of triphenylphosphine hydrobromide (1.1 equiv.) in dichloromethane. After 2h at 0°C and 1h at ambient temperature, the mixture was neutralized with methanolic NaOMe, filtered and the solvent evaporated. Removal of excess triphenylphosphine by ether trituration afforded essentially pure Wittig salt (Scheme I).

Scheme I



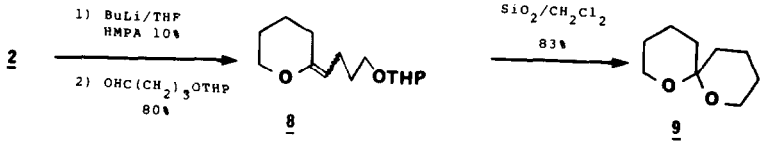
The long-chain, ketonic sex pheromone 7 of the Douglas-fir tussock moth[7] was assembled by condensing the deep red ylide of 2 with decanal (-78°C to R.T. over 6h) and conversion of the resultant enol ether 4 to δ-iodoketone 5 using Me_3SiCl/NaI[8]. Introduction of the cis-olefin via cuprate 6[9] generated 7 in 42% overall yield[10] (Scheme II).

Scheme II



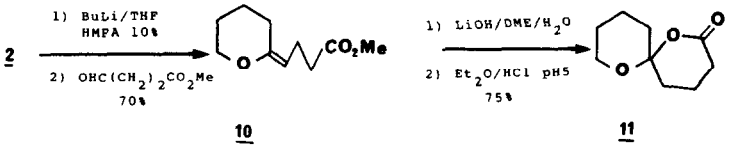
Pheromone 9, isolated from the olive fly Dacus oleae[11], is representative of the growing collection of naturally occurring spiroketals[12]. Convenient access to this class was demonstrated by a brisk synthesis of racemic 9 [5f,6] in 66% overall yield involving Wittig condensation of 2 with THP protected γ-hydroxybutanal followed by silica gel mediated cyclization of enol ether 8 (Scheme III).

Scheme III



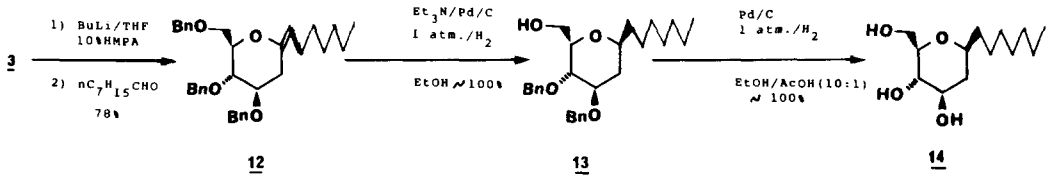
This basic theme was extended by uniting the ylide of 2 with methyl 3-formylpropionate resulting in enol ether 10 (Scheme IV). Saponification and acid catalyzed cyclization evolved oxaspirolactone 11, a key structural element[13] in several plant and insect pheromones[14].

Scheme IV



Synthesis of C-glycoside 14 outlined in Scheme V commenced with Wittig condensation of 3 and octanal. Catalytic reduction of the resultant enol ether 12 in the presence of 1% Et_3N furnished β-C-octyl-D-glucopyranoside 13 exclusively. Reduction in the absence of base was accompanied by exo/endo isomerization[5f] of the extremely labile enol ether and resulted in a mixture of α- and β-isomers. Removal of the remaining benzyls afforded 14 in 78% overall yield. This methodology complements the usual approach to C-glycosides based on nucleophilic alkyl addition at C-1[15]. As expected by analogy with structurally related compounds[16], 14 exhibits interesting detergent properties and may prove useful for the activation and/or solubilization of membrane proteins.

Scheme V



The phosnium bromide preparation and transformations highlighted in the foregoing syntheses can be recommended for their versatility and convenience. Additional applications expanding the scope of Wittig olefinations leading to enol ethers of value in natural products synthesis will be reported in due course.

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