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A NEW ROUTE TO STABILIZED YLIDES: A ONE-POT POLYENE SYNTHESIS

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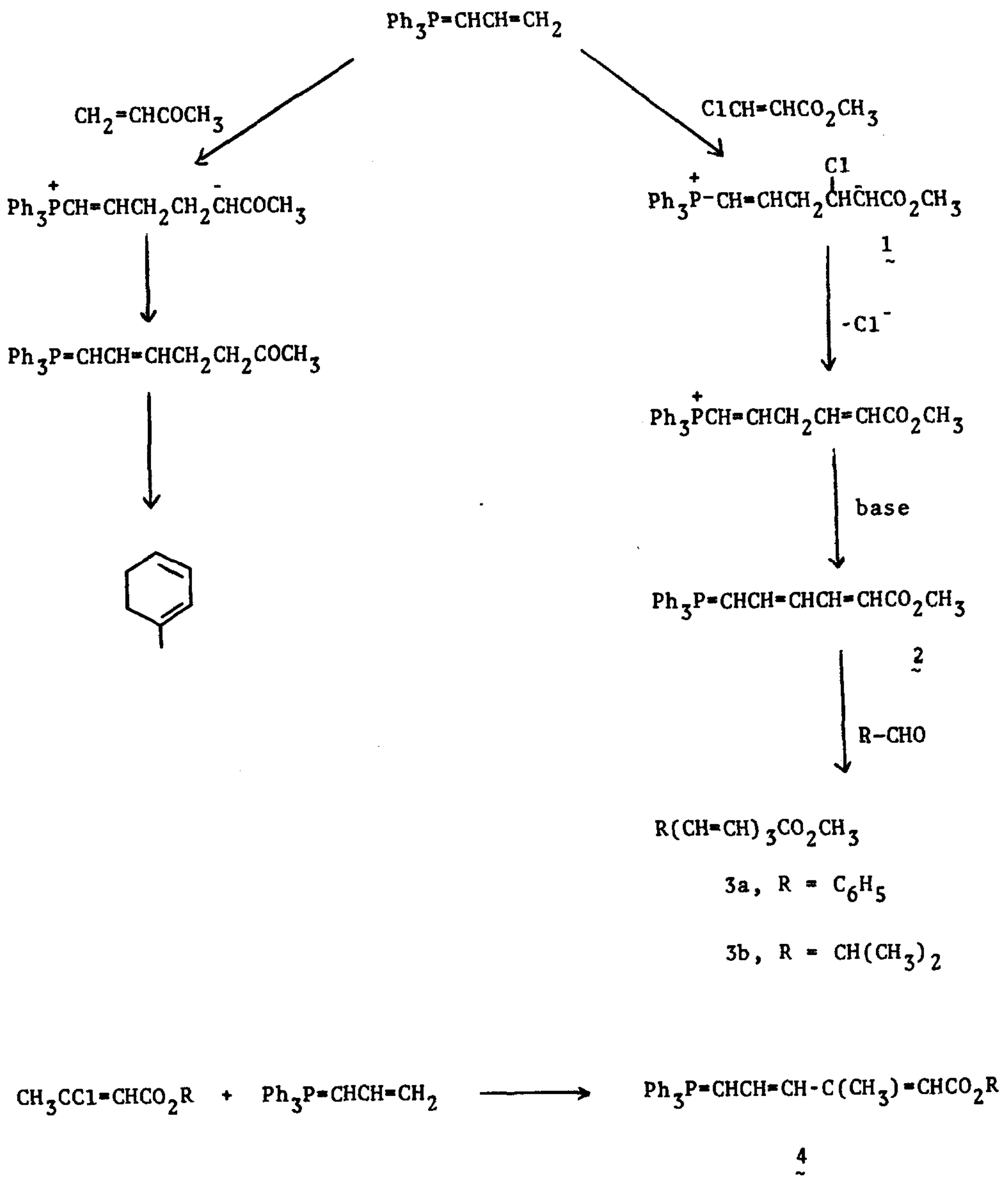
Allylic ylides react with electrophiles at both the α and γ carbons, depending on the substrate and the reaction conditions.[1] In the case of α,β-unsaturated ketones, the preferred mode of reaction involves bond formation between the enone β-carbon and the ylide γ-carbon. Subsequent proton transfer and internal Wittig cyclization completes an elegantly simple synthesis of cyclohexadienes (Fig. 1).[2]

We have found that allylidenetriphenylphosphorane adds analogously to β-chloroacrylate esters and related Michael acceptors, presumably to give intermediates such as 1. Subsequent loss of chloride and deprotonation by base (typically, excess starting ylide in these experiments) converts 1 into the stabilized ylide 2. Treatment of the crude product solution with benzaldehyde affords the expected Wittig product, all trans isomer 3a[3] (84% isolated yield based on chloroacrylate). Similar trapping of crude 2 with isobutyraldehyde results in 3b (67%, 1:1.5 mixture of cis:trans isomers).

The same "one pot" procedure[4] was employed with other α,β-unsaturated β-chlorocarbonyl compounds as summarized in Fig. 2. It is apparent that conjugated polyene esters or ketones are easily prepared in acceptable yield, provided that the stabilized ylide is trapped with an aldehyde. The low yield of cyclohexanone adduct 5 is consistent with the reluctance of related ylids to react with ketones.[5]

Addition of allylidenetriphenylphosphorane to methyl β-chlorocrotonate is of special interest because the resulting ylide 4 corresponds to the terminal

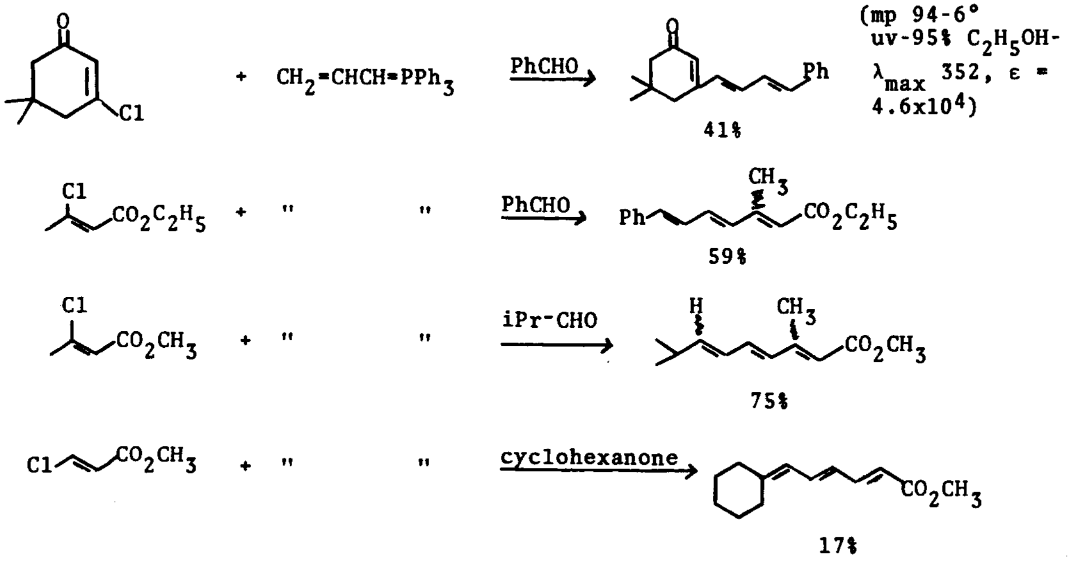
Fig. 1


Ph3P=CHCH=CH2
CH2=CHCOCH3
ClCH=CHCO2CH3
Ph3P+CH=CHCH2CH2CH−COCH3
Ph3P+-CH=CHCH2CH(Cl)C−HCO2CH3
1
Ph3P=CHCH=CHCH2CH2COCH3
-Cl−
Ph3P+CH=CHCH2CH=CHCO2CH3
base
Ph3P=CHCH=CHCH=CHCO2CH3
2
R-CHO
R(CH=CH)3CO2CH3
3a, R = C6H5
3b, R = CH(CH3)2
CH3CCl=CHCO2R + Ph3P=CHCH=CH2
Ph3P=CHCH=CH-C(CH3)=CHCO2R
4

carbons of the Vitamin A methyl ester side chain. However, 4 does not appear to be suited for stereoselective synthesis of isoprenoid polyenes. Trapping the ylide with isobutyraldehyde affords comparable amounts of four isomers having uv λ_{max} in the 295-305 nm range. Apparently, elimination of chloride ion from the zwitterionic intermediate generates both E and Z isomers at the trisubstituted double bond of 4. Each of the E, Z isomers then affords a pair of cis,trans isomers in the Wittig condensation step.

The net effect of the observed reactions is to replace a γ-proton of allylidenetriphenylphosphorane by the β-carbon of an unsaturated ester or ketone. The procedure allows facile synthesis of compounds having at least three double bonds conjugated with a carbonyl function. We have found no evidence for the formation of cross-conjugated isomers which might be derived from initial α-capture of allylidenetriphenylphosphorane.

Figure 2



(mp 94-6° uv-95% C_2H_5OH- λ_{max} 352, ε = 4.6×10^4)

5

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4. In a typical experiment, allyltriphenylphosphonium bromide (0.38 g) was stirred in dry THF (10 ml) under nitrogen and treated with lithium diisopropylamide (1.4 ml, 0.73 N in hexane-THF). After 30 min at 20°, methyl cis-3-chloropropenoate (0.03 g) was added dropwise. The mixture was stirred 2 hrs at room temperature and quenched with excess benzaldehyde (overnight). Chromatography of the product over silica gel after aqueous workup gave **3** (0.045 g, 84%).
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