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New Insights on the Reaction of Alkyl 3-Oxo-4-(triphenylphosphoranylidene)butanoate and Aldehydes under Concentrated Condensation Conditions. One-pot Synthesis of Highly Functionalised 6-Oxocyclohex-4-ene-1,3-dicarboxylates

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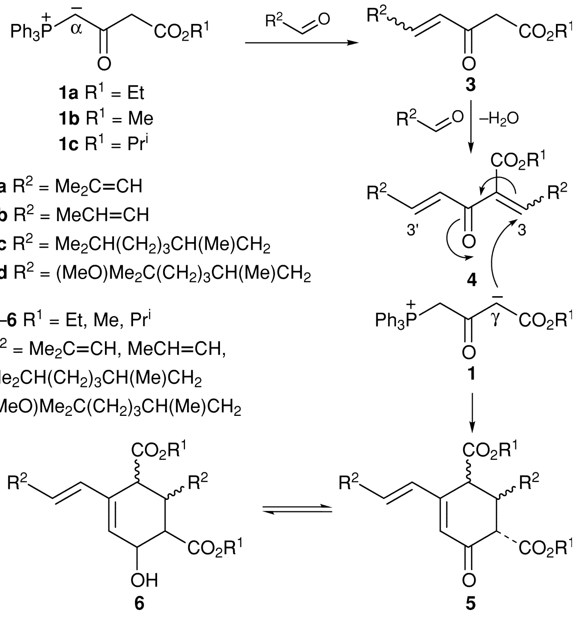
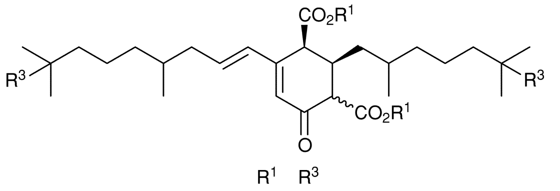
A general method for the synthesis of substituted cyclohexenones **5** from the condensation of acetoacetate phosphonium ylide **1** and saturated and unsaturated aldehydes **2**, without activation, is described.

Condensation of alkyl 3-oxo-4-(triphenylphosphoranylidene)-butanoate **1**[1,2] and α,β-unsaturated aldehydes 3-methylbut-2-enal **2a**[5] and but-2-enal **2b** with little or no solvent, gave a diastereomeric mixture of three of the four possible 6-oxocyclohex-4-ene-1,3-dicarboxylates **5a** and **5b** as the main condensation products in yields of 31 and 27% respectively. Two of the three diastereomers of **5** were in equilibrium with only one diastereomer of the enoldiester **6** (Scheme A). The reaction mixture also contained the expected γ,δ-unsaturated-β-keto esters **3** in low yield and the *trans*-aldo product **4** as the alkyl 2*H*-pyran-5-carboxylates. Condensations of **1** with saturated aldehydes 3,7-dimethyloctanal **2c** and 7-methoxy-3,7–dimethyloctanal **2d** gave also cyclohexenonedicarboxylates **5c** and **5d** as the main products in yields of 52 and 40% respectively. However, when the reactions were performed in dilute solutions γ,δ-unsaturated-β-keto esters **3** were the main products.



Scheme A Condensation of phosphonium ylide **1** and saturated or unsaturated non-aromatic aldehydes **2**



	R^1	R^3
5c	Me	H
5d	Pr^i	OMe
5e	Et	H

Scheme B

The 2,4-disubstituted-6-oxocyclohex-4-ene-1,3-dicarboxylates **5** were obtained *via* a cascade Wittig, aldol, Michael–Wittig condensation sequence. Only C^3–C^{γ} Michael attack takes place between the intermediate cross-conjugated ketoester **4** and the γ-ylide of the phosphonium ylide **1**, no product formation occurs as the result of a $C^{3'}C^{\gamma}$ Michael attack (Scheme A). The diesters **5d** and **5e** obtained showed ectoparasiticidal activity (Scheme B).

Although we are now more confident to predict the outcome of the condensation between an aldehyde and alkyl 3-oxo-4-(triphenylphosphoranylidene)butanoate **1**, this ylide **1**, under classical Wittig condensation conditions, remains a rather challenging phosphonium ylide to use.

Techniques used: ^1H and ^{13}C NMR, EI-MS, IR, UV–VIS, MO calculations

Tables: 10 (^1H and ^{13}C NMR data; yields of products; conformational energies)

Fig. 1: Typical model structure used for MO calculations

Schemes: 3

References: 16

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