β-Diphenylphosphinoyl Ketones ($Ph_2PO{\cdot}CH_2CH_2CO{\cdot}R$): Stable Reagents for β-Ketocarbanions

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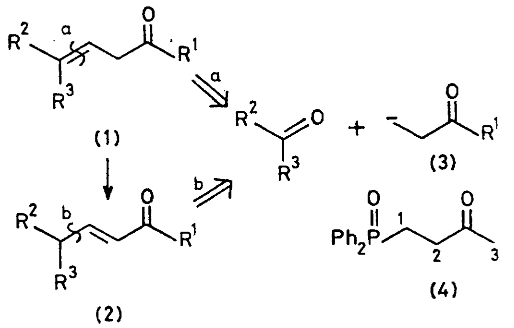
Summary Acetals of the title compounds, available by five different routes, act as homoenolate equivalents by the Horner–Wittig reaction.

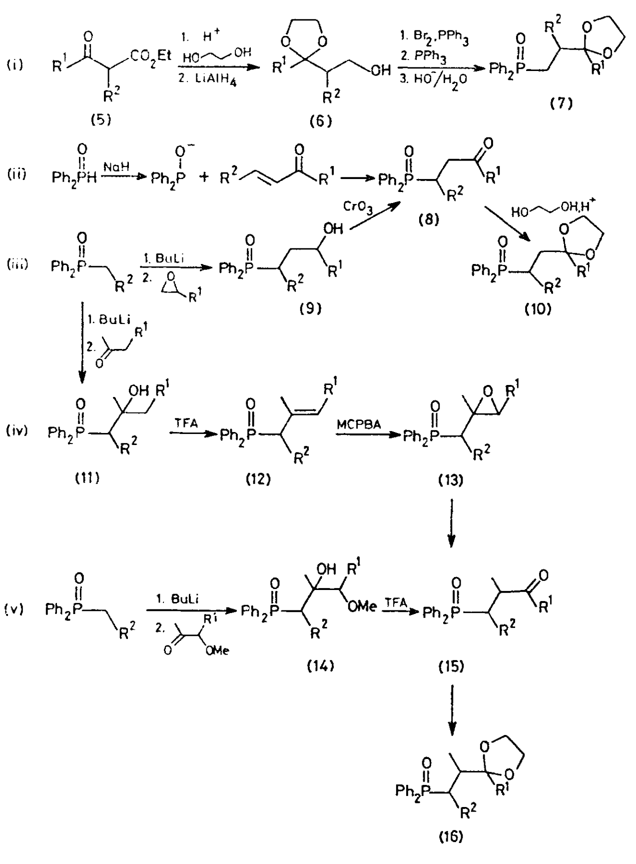
Conventional disconnection [a in (**1**)] of β,γ-unsaturated carbonyl compounds leads to the homoenolate ion (**3**). Reagents available for this synthon include those based on sulphur[1] and Grignard reagents from protected β-halogeno-ketones.[2] The unconventional disconnection [b in (**2**)] of conjugated enones leads to the same synthon.



We report that acetals of β-diphenylphosphinoyl (Ph_2PO) ketones (**4**), available by five different routes (Scheme) are homoenolate equivalents by their Horner–Wittig reaction with aldehydes and ketones. In routes (i) and (ii) (Scheme) compounds formed by conventional carbonyl condensations are given umpolung[1] by the addition of the Ph_2PO group. β-Keto esters (**5**) can be protected and reduced[2] [route (i)] to give the alcohols (**6**) and hence, *via* the phosphonium salts[3] which are not isolated, the acetals (**7**) *e.g.* (**7**; $R^1 = Me$, $R^2 = H$); 46% from (**6**). This route is particularly suitable for reagents (**7**) having substituents on C-2 and C-3. The anion of diphenylphosphine oxide [route (ii)] adds directly to enones[4] to give reagents (**8**) substituted on C-1 and C-3, *e.g.* (**8**; $R^1 = Et$, $R^2 = H$, 55%; $R^1 = R^2 = Me$, 58%).

In routes (iii) to (v) we use the Ph_2PO group to assemble the carbon skeleton before the carbonyl group is introduced. Addition of alkyl-phosphine oxide anions to epoxides [route (iii)] gives alcohols (**9**), *e.g.* (**9**; $R^1 = Ph$, $R^2 = H$, 87%), converted by Jones oxidation into the ketones (**8**), *e.g.* (**8**; $R^1 = Ph$, $R^2 = H$, 96%), with the same substitution pattern as those derived from route (ii).

We have already described[3] the addition of ketones to primary alkyl-phosphine oxides and the dehydration of the adducts (**11**) with trifluoroacetic acid (TFA) to give allyl-phosphine oxides (**12**). The same sequence [route (v)] with α-methoxy ketones† gives adducts (**14**), *e.g.* (**14**; $R^1 = R^2 = Me$, 75%), which give the transposed ketones (**15**) with TFA, *e.g.*, (**15**; $R^1 = R^2 = Me$, 80%), presumably *via* a vinyl ether. Direct conversion of the adducts (**14**) into the acetals (**15**) by treatment with toluene-*p*-sulphonic acid (TsOH) in refluxing benzene first alone, then with ethylene glycol, gave higher yields, *e.g.* (**16**; $R^1 = R^2 = Me$); 85% from (**14**).



Scheme

Alternatively [route (iv)], the allyl-phosphine oxides (**12**) made by this route or by Ph_2PO migration,[3] gave crystalline epoxides (**13**) with *m*-chloroperbenzoic acid (MCPBA), *e.g.* (**13**; $R^1 = Me$, $R^2 = H$, 61%), which in some cases rearrange to the ketones (**15**) with TFA or BF_3, *e.g.* (**15**; $R^1 = Me$, $R^2 = H$, 90%). In other cases this reaction gave poor yields, *e.g.* on (**13**; $R^1 = Pr^i$, $R^2 = H$). Routes (iv) and (v) are suitable for compounds with substituents on C-1, C-2, and C-3.

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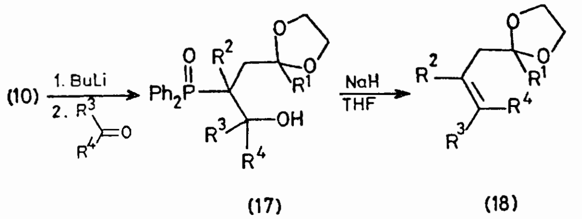
† Conveniently made from adducts of aldehydes and acetylene by methylation with dimethyl sulphate and hydration of the triple bond (D. Guillerm-Dron, M. L. Capmau, and W. Chodkiewicz, *Bull. Soc. chim. France*, 1973, 1417).



Where the ketone is isolated, as in routes (ii) and (iii), conversion into the crystalline acetal is near quantitative, [*e.g.* (**8**) → (**10**); $R^1 = Ph$, $R^2 = H$; 91%]. The acetals (**7**), (**10**), and (**16**) form anions [BuLi, tetrahydrofuran (THF)] which add to aldehydes and ketones in the usual way[3] to give adducts (**17**), *e.g.* (**17**; $R^1 = Ph$, $R^2 = H$, $R^3 = R^4 = Me$, 93%; $R^1 = R^2 = Me$, $R^3 = Ph$, $R^4 = H$, 81%), which eliminate Ph_2PO^- on treatment with NaH in THF to give the Horner–Wittig product (**18**), *e.g.* (**18**; $R^1 = Ph$, $R^2 = H$, $R^3 = R^4 = Me$, 95%; $R^1 = R^2 = Me$, $R^3 = Ph$, $R^4 = H$, 96%). Deprotection of the products (**18**) is straightforward.

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[4] P. F. Cann, S. Warren, and M. R. Williams, *J.C.S. Perkin I*, 1972, 2377.