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A FACILE PROCEDURE FOR THE SYNTHESIS OF α,β-UNSATURATED ALDEHYDES BY THREE CARBON HOMOLOGATION

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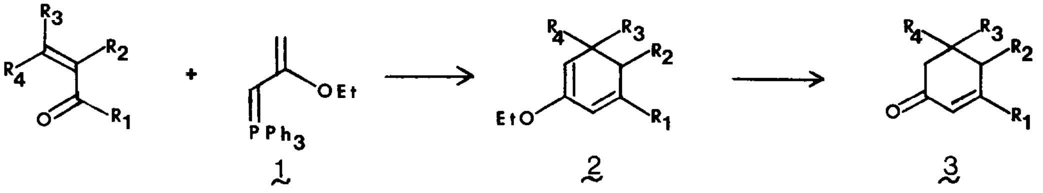
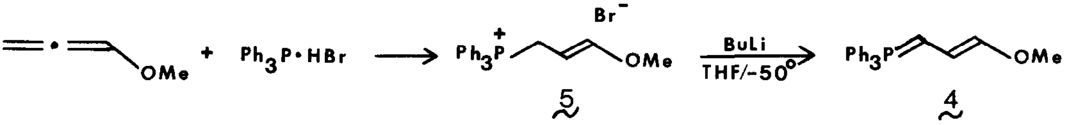
Despite the plethora of procedures for the conversion of carbonyl compounds into aldehydes or ketones containing one or two additional carbon atoms, there is a relative paucity of synthetic methodology for the extension of a carbonyl function by three carbon atoms.[1] We now wish, therefore, to report a facile, one pot procedure for the three carbon homologation of aldehydes and ketones to α,β-unsaturated aldehydes or 1-methoxy-1,3-butadienes.

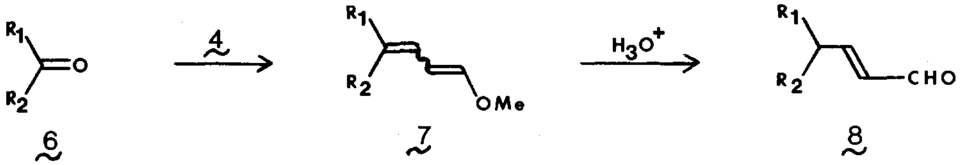
During the course of a recent investigation of the reactions of a new class of synthetic reagents, heteroatom-substituted allylidenephosphoranes, we found that 2-ethoxyallylidene triphenylphosphorane (1) was a convenient reagent for the annulation of 2-ethoxy-1,3-cyclohexadienes 2 and cyclohexenones 3 onto α,β-unsaturated ketones.[2] This discovery prompted further studies to evaluate the possible synthetic utility of other related alkoxyallylidene phosphoranes as reagents for organic synthesis.



Another member of this new class of compounds is 3-methoxyallylidene triphenylphosphorane (4) which may be easily generated by treating 3-methoxy-2-propenyl triphenylphosphonium bromide (5) with *n*-butyllithium. While a number of possible syntheses of the phosphonium salt 5 may be envisioned, the most efficient procedure involves the reaction of methoxyallene[3] with triphenylphosphonium bromide[4] which produces 5[5] in 68% yield.



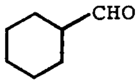
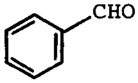
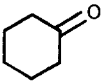
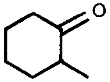
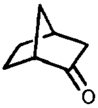
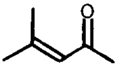
3-Methoxyallylidene triphenylphosphorane (4) reacts readily with simple carbonyl compounds 6 to give 1-methoxy -1,3-butadienes 7[6,7] which may be isolated and utilized as synthetic intermediates in a variety of subsequent transformations.[8] Alternatively, the methoxybutadienes 7 may be hydrolyzed *in situ* with aqueous acid to yield directly the *trans*-α,β-unsaturated aldehydes 8.[7] Using this facile, one pot procedure, a variety of simple



aldehydes and ketones may be converted into α,β-unsaturated aldehydes or 1-methoxy-1,3-butadienes with three carbon homologation in good overall yields (see Table). In unexpected contrast to 2-ethoxyallylidene triphenylphosphorane (1), the ylid 4 appears to react in a normal Wittig fashion with α,β-unsaturated ketones by 1,2-addition at the α-carbon of the allyl moiety to give 1-methoxy-1,3,5-hexatrienes (*e.g.*, entry 8).[9]

The following experimental procedure is representative of this conversion: To a well stirred suspension of 3-methoxy-2-propenyl triphenylphosphonium bromide (5) (5.20 g, 12.6 mmol) in anhydrous tetrahydrofuran (THF) (50 ml) under dry nitrogen at -50° was added *n*-BuLi in hexane (12.6 mmol). Upon completion of the addition, the reddish-orange mixture was stirred at -25° for 2 hr. The solution of 3-methoxyallylidene triphenylphosphorane was then cooled to -50°, and a solution of cyclohexanone (0.81 g, 8.3 mmol) in anhydrous THF (5 ml) was slowly added. The resulting mixture was allowed to warm slowly to room temperature and then stirred overnight. At this point the work-up procedure may be altered to obtain either a 1-methoxy-1,3-butadiene 7 or an α,β-unsaturated aldehyde 8. For example, addition of saturated brine followed by extractive workup with ether gave 3-cyclohexylidene-1-methoxypropene (75%):

Table. Preparation of 1-Methoxybutadienes **7** and α,β-Unsaturated Aldehydes **8**

Entry	Starting Carbonyl **6**	% Yield of **7**	% Yield of **8**[a,b]
1	$n\text{-}C_6H_{13}CHO$		64
2			73
3		75[c]	
4	$(CH_3)_2CH(CH_2)_2COCH_3$		40
5		75	74
6			52[d]
7			65[d]
8		41[c]	

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[a] Greater than 95% α,β-unsaturated by NMR; [b] On the basis of NMR coupling constants of vinyl protons (J ≈ 15Hz), only *trans* alkene formed; [c] Obtained as mixture of geometric isomers; [d] Obtained as a mixture of diastereomers.

bp 87-88° (2.3 mm); NMR ($CDCl_3$/TMS) δ6.50 (m, 1H), 5.65 (m, 2H), 3.54 (s, 3H), 2.10 and 2.18 (two br overlapping s, 4H) and 1.52 (br s, 6H); Exact mass. Calcd for $C_{11}H_{12}O$, 160.0888. Found, 160.0892. On the other hand, addition of 1N hydrochloric acid (50 ml) to the above solution of the crude diene, followed by heating at reflux for 10 hr[10] and extractive work-up with ether gave 3-cyclohexyl-2-propenal (74%): bp 73-75° (4.0 mm); NMR ($CDCl_3$/TMS) δ9.54 (d, 1H, J = 7.5Hz), 6.82 (d of d, 1H, J = 15Hz, 6Hz), 6.06 (d of d, 1H, J = 15 Hz, 7.5Hz), 1.2-2.3 (m, 10H); MS, *m/e* = 138, 109, 94, 81 (base), 67; mp of

2,4-DNP (ethanol) 212-213°, [lit.,[11] 204-206°].

Efforts to further explore the synthetic utility of this and other hetero-substituted allylidene triphenylphosphoranes are under active investigation and will be reported independently.

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References and Notes

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3. S. Hoff, L. Brandsma and J. Arens, Recl. Trav. Chim. Pays-Bas, 87, 916 (1968).
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5. Mp 209-210°; NMR ($CDCl_3$/TMS): δ 3.46 (s, 3H); 4.63 (m, 3H), 6.85 (m, 1H), 7.78 (m, 15H). Anal: Calcd for $C_{22}H_{22}OPBr$: C, 63.94; H, 5.37. Found: C, 63.76; H, 5.21.
6. A related synthesis of other 1-heteroatom-substituted 1,3-butadienes has been reported. See G. Lavielle and G. Sturtz, Bull Soc. Chim. Fr., 1369 (1970).
7. All compounds were adequately characterized by spectral methods (IR, NMR and MS), and all new compounds gave satisfactory high resolution mass spectral and/or combustion analytical data.
8. For a review of the use of 1-alkoxybutadienes in organic synthesis see S. M. Makin, Russian Chem. Rev., 38, 237 (1969).
9. Other experiments have shown that the ylid 4 also reacts with other α,β-unsaturated ketones such as 3-penten-2-one and 1-acetylcyclohexene predominantly at the α-carbon.
10. Hydrolysis under a variety of milder reaction conditions failed to give any appreciable amount of the β,γ-isomer.
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