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PREPARATION OF α-OXYGENATED PHOSPHINE OXIDES FROM CHLORODIPHENYLPHOSPHINE

Mehran Maleki, and Allen Miller*

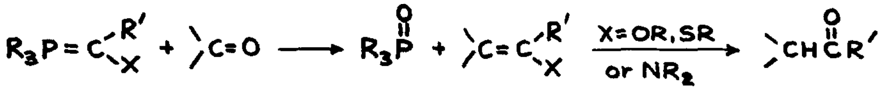
Chemistry Department, The University, Dundee DD1 4HN, Scotland.

O. William Lever, Jr.

Department of Organic Chemistry, Burroughs Wellcome Co.,
Research Triangle Park, N.C. 27709, U.S.A.

SUMMARY A range of α-alkoxyphosphine oxides, including novel α-methoxyallyl oxides, are readily prepared from chlorodiphenylphosphine and acetals.

A number of interesting applications of the Wittig and related reactions centre on the reactions of α-functionalised ylids, from which various enol derivatives may be prepared.[1] In such circumstances, these ylids behave as acyl anion equivalents,[2] as shown by the sequence in scheme 1. The synthetic value of this type of Wittig reaction is however somewhat limited, largely because its efficiency is extremely variable. Unfortunately, the situation with ylids derived from α-substituted phosphonates is even worse, since the elimination step, leading to alkene, is generally favoured only when the α-hetero substituent is anion-stabilising.[3]

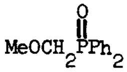
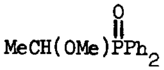
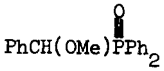
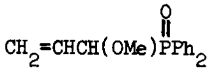
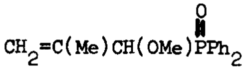
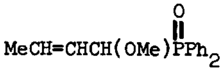
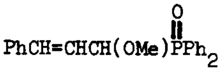
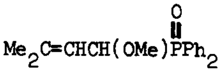
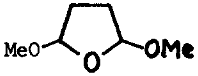
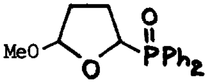
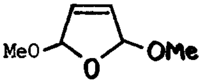
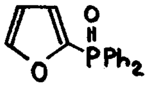
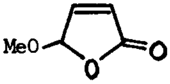


$$R_3P{=}C(R')X + {>}C{=}O \longrightarrow R_3P{=}O + {>}C{=}C(R')X \xrightarrow[\text{or } NR_2]{X=OR,SR} {>}CHC(=O)R'$$

SCHEME 1

Although the ability of phosphine oxide based ylids to give alkenes under Wittig-type conditions has been recognised for many years,[4] such ylids were initially of little utility in synthesis. In the last five years, however, it has become clear that ylids from phosphine oxides hold several advantages in Wittig chemistry, notably where enol derivatives are required. Recent successes in the preparation of enol-ethers,[5] enamines,[6] vinyl sulphides[7] and polyenes[8] suggest that this Wittig-Horner sequence is very efficient and that it is of wide applicability. In turn, this depends upon the availability of a range of α-functionalised phosphine oxides, and we now report studies of a somewhat neglected route to one example of this type of structure - the α-alkoxyalkyldiphenylphosphine oxides (1).

TABLE α-Alkoxyphosphine Oxides (1) from Chlorodiphenylphosphine and Acetals (Scheme 2).

Acetal	Phosphine Oxide (1)[a]	Yield (%)[b]	m.p. (°C)
$CH_2(OMe)_2$	 $\mathrm{MeOCH_2\overset{\overset{O}{\|}}{P}Ph_2}$	25	114-116
$MeCH(OMe)_2$	 $\mathrm{MeCH(OMe)\overset{\overset{O}{\|}}{P}Ph_2}$	85	60-62
$PhCH(OMe)_2$	 $\mathrm{PhCH(OMe)\overset{\overset{O}{\|}}{P}Ph_2}$	98	172-174
$CH_2{=}CH.CH(OMe)_2$	 $\mathrm{CH_2{=}CHCH(OMe)\overset{\overset{O}{\|}}{P}Ph_2}$	62	90-91.5
$CH_2{=}C(Me)CH(OMe)_2$	 $\mathrm{CH_2{=}C(Me)CH(OMe)\overset{\overset{O}{\|}}{P}Ph_2}$	70	113-114
$MeCH{=}CHCH(OMe)_2$	 $\mathrm{MeCH{=}CHCH(OMe)\overset{\overset{O}{\|}}{P}Ph_2}$	50	92-93
$PhCH{=}CH.CH(OMe)_2$	 $\mathrm{PhCH{=}CHCH(OMe)\overset{\overset{O}{\|}}{P}Ph_2}$	90	105-107
$Me_2C{=}CH.CH(OMe)_2$	 $\mathrm{Me_2C{=}CHCH(OMe)\overset{\overset{O}{\|}}{P}Ph_2}$	77	108-110
		90	100.5-102
	[only ]	-	-
	no reaction	-	-

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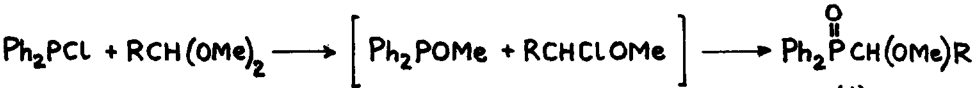
[a] Full microanalytical and spectroscopic characterisation of these oxides has been obtained and will be reported in detail elsewhere.

[b] Quoted yields are after recrystallization.

Our work is based on the well established[9] reaction of phosphorus trichloride, or its partial esters, with acetals. With few exceptions,[10] this has not been applied to the preparation of α-alkoxyphosphine oxides (1), and we find this reaction to proceed in good yield and in a one-pot sequence for chlorodiphenylphosphine and a range of acetals, as shown in scheme 2. Perhaps the most interesting aspect of this reaction is that it works extremely well with allylic acetals (i.e. acetals of α,β-unsaturated aldehydes), giving only one phosphine oxide. These oxides are all crystalline compounds which handle and store well. Details of individual oxides appear in the Table, and a general experimental procedure is outlined below.



$$Ph_2PCl + RCH(OMe)_2 \longrightarrow \left[Ph_2POMe + RCHClOMe \right] \longrightarrow Ph_2\overset{O}{\overset{\|}{P}}CH(OMe)R$$

(1)

SCHEME 2

One of the attractions of this route to the oxides (1) is that it avoids the direct handling of toxic α-chloroethers, such as chloromethyl methyl ether. Unfortunately the reaction of dimethoxymethane with chlorodiphenylphosphine, in which chloromethyl methyl ether is an intermediate, yields bis(methoxymethyl)diphenylphosphonium chloride, along with the desired oxide (1, R=H). Two other structural limitations of scheme 2 are revealed by the last two entries in the Table.

Preparation of α-Alkoxyallylphosphine Oxides; Typical Procedure

Although it is not essential to use dried glassware and redistilled reagents, yields are improved if this is done. Chlorodiphenylphosphine (0.1 mol) in dichloromethane (1 ml/g) is added dropwise under nitrogen to the acetal (0.1 mol) with stirring at 0°C (bath temperature). The mixture is stirred for 1 h at 0°C after the addition is complete and then at 20°C for a further period of 2-14 h. Evaporation of dichloromethane and residual chloromethane leaves an oily residue (∿100%), which, as judged by ^{1}H NMR and by IR spectra, is essentially pure oxide (1). The oxides are crystallized from toluene-petrol (40-60°C) until they give sharp melting points and single-spot TLC's.

Overall, this work confirms the wide applicability of the acetal-chlorophosphine route to phosphine oxides. In particular, the presence of the allyl group in (1) allows the possibility of further functionalisation prior to a Wittig-Horner reaction, and, moreover, the possibility of a new route to 2-alkoxy-1,3-dienes.[11] In turn, this may lead to sequences in which the oxides (1) act as vinyl acyl anion equivalents.[12] These aspects are currently being investigated.

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10. We are aware of only three examples in the literature (see refs. 9a, 9b) and these use either 1,1-dimethoxyethane or dimethoxymethane as acetal.
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