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THE CARBONYL INSERTION REACTIONS OF MIXED TERVALENT PHOSPHORUS-ORGANOSILICON REAGENTS

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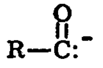
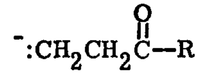
In conjunction with our general interest in the development of synthetic operations which reverse the normal polar reactivity patterns of the carbonyl function,[1] we have been focusing our attention on carbonyl derivatives which could serve as operational equivalents to the hypothetical carbanions 1 and 2.[2,3] In this regard we have been engaged in the development of organosilicon reagents 3 containing potential carbanion-stabilizing functions, A, which will undergo facile carbonyl addition (eq. 1). In principle, such carbonyl derivatives, upon metalation, should serve as valuable carbon nucleophiles in organic synthesis. During the course of this study, a series of brief notes appeared on the reaction of tervalent phosphorus reagents 4a and 4b with saturated aldehydes and ketones (eq. 2) to give phosphonates 5a[4] and phosphonamides 5b[5] respectively (Method A). A complementary method for converting aliphatic and aromatic aldehydes into α-siloxyphosphonates (eq. 3) has been described in the patent literature (Method B).[6]



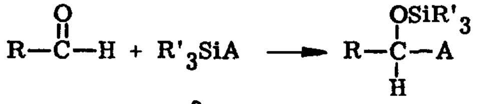
$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{:}^{-}$

1



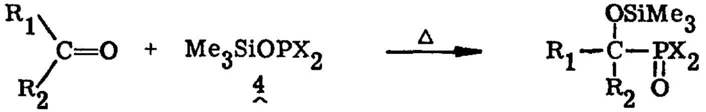
$^{-}{:}CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}{-}R$

2



$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}H + R'_3SiA \longrightarrow R{-}\underset{\underset{\displaystyle H}{|}}{\overset{\overset{\displaystyle OSiR'_3}{|}}{C}}{-}A \qquad (1)$$

3



$$\begin{matrix}R_1\\ \end{matrix}\!\!\!\!\diagdown_{C=O}^{} \; R_1R_2C{=}O + Me_3SiOPX_2 \xrightarrow{\Delta} R_1{-}\underset{\underset{\displaystyle R_2}{|}}{\overset{\overset{\displaystyle OSiMe_3}{|}}{C}}{-}\underset{\underset{\displaystyle O}{\|}}{P}X_2$$

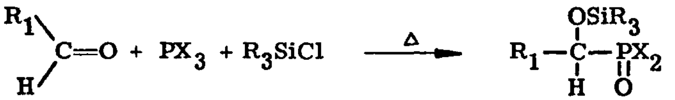
4

a, X = O-Alkyl

b, X = NEt_2

5

Method A (2)



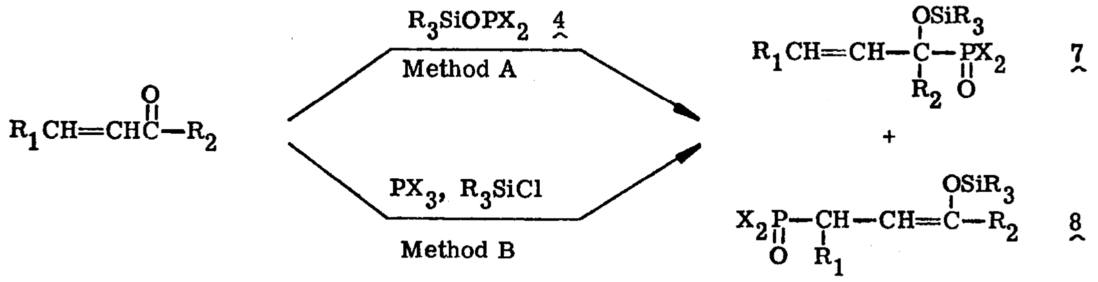
$$R_1(H)C{=}O + PX_3 + R_3SiCl \xrightarrow{\Delta} R_1{-}\underset{\underset{\displaystyle H}{|}}{\overset{\overset{\displaystyle OSiR_3}{|}}{C}}{-}\underset{\underset{\displaystyle O}{\|}}{P}X_2$$

6

Method B (3)

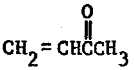
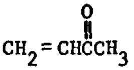
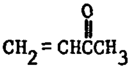
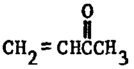
The purpose of this communication is to report our observations on the scope of these carbonyl addition processes with α,β-unsaturated ketones and aldehydes. Of particular interest in this study has been the regiochemistry (1,2 vs 1,4-addition) and probable mechanism of these addition processes, a point which has not been dealt with in previous studies (Scheme I).

Scheme I



Three silicon-phosphorus reagents **4** were prepared for study. Dimethyl trimethylsilyl phosphite [TMSOP(OMe)$_2$] and dimethyl triethylsilyl phosphite [TESOP(OMe)$_2$] were prepared by known procedures.[4b] Triethylsilyl N,N,N',N'-tetramethyl phosphorodiamidite [TESOP(NMe$_2$)$_2$] was prepared from N,N,N',N'-tetramethylphosphorodiamido chloride[7] and triethylsilanol in ether/triethylamine (bp 66-74 °C, 0.02 mm; 55% yield).[8] The reactions of the mixed silicon-phosphorus reagents **4** (Method A) with a series of α,β-unsaturated aldehydes and ketones were carried out with one equivalent of each reagent either neat or in THF under an inert atmosphere. The aldehyde addition reactions generally proceeded at a convenient rate at ambient temperatures while ketonic substrates required heating. The complementary addition reactions employing the phosphite esters, PX_3, and chlorosilanes (Method B), as described by Birnum,[6] were carried out with stoichiometric quantities of each reagent, neat, at the indicated temperatures in sealed ampules (Table). Qualitatively, the relative reactivities of the tervalent phosphorus reagent, PX_3, followed the general order: $ROP(NMe_2)_2 \gg ROPPh_2 > (RO)_3P$ (c.f. Entries 10-12). This trend is consistent with the relative nucleophilicities of related phosphorus derivatives towards alkyl halides.[9] The possibility that the 1,2 and 1,4-adducts **7** and **8** might be interconverted thermally was eliminated by the following experiment: The crotonaldehyde 1,2 and 1,4-adducts (Entry 5, Table) were individually heated (200 °C, 24 h), and no interconversion was detected. The high thermal stability observed in this instance suggests that the 1,2:1,4-adduct ratios reported in the Table are a consequence of kinetic control during the addition process. From a mechanistic standpoint the two methods reported herein differ in that Method A involves intramolecular silicon transfer during the addition process.[10] Furthermore, we have determined that under the conditions employed for Method B, the mixed silicon phosphorus reagent **4** is not an intermediate. One rational mechanism for the 1,2-addition of the tervalent phosphorus-silicon reagent **4** to carbonyl substrates is illustrated in Scheme II.[10] In those cases where 1,4-addition is possible, several observations suggest that addition proceeds via the oxaphospholenes **10** (Method A) and **11** (Method B). First, the

Table. Addition Reactions of Mixed Phosphorus Reagents to Carbonyl Substrates (Scheme I).[8]

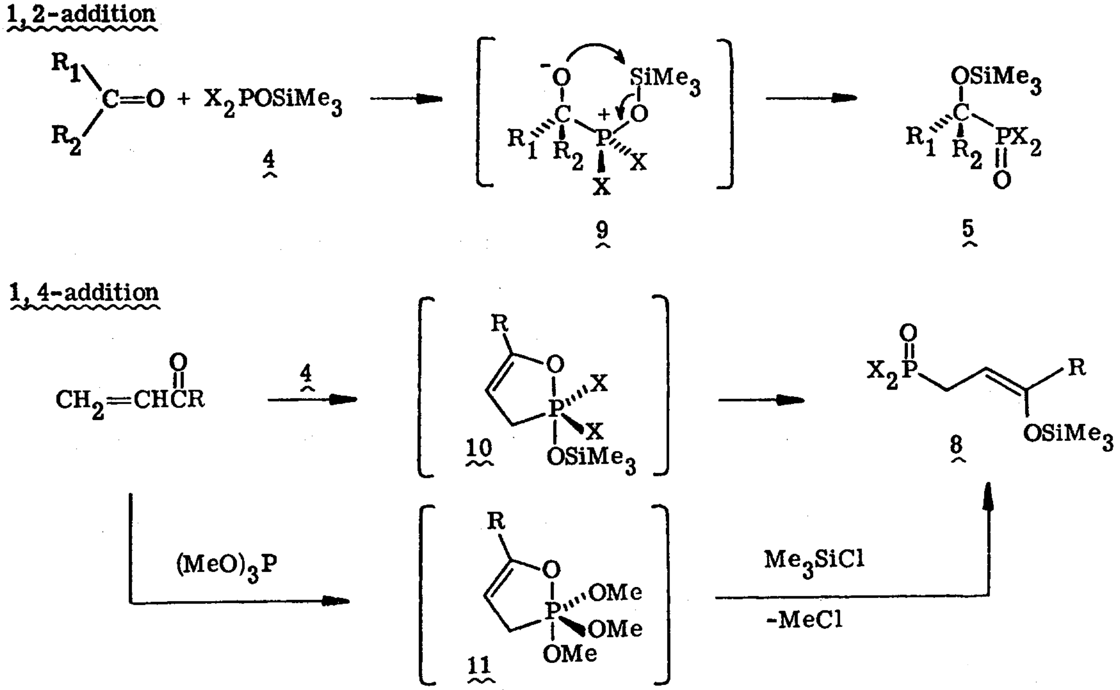
Entry	Substrate	PX_3 (Method)	Conditions[a]	% Yield[b]	Ratio (7:8) 1,2:1,4-addition
1	$CH_2{=}CHCHO$	$TMSOP(OMe)_2$ (A)	25°, 12 h	88	47:53
2	$CH_2{=}CHCHO$	$(MeO)_3P/TMSCl$ (B)	25°, 4 h	70	> 99:1
3	$CH_2{=}CHCHO$	$TESOP(NMe_2)_2$ (A)	0°, 1/4 h[c]	90	> 99:1
4	$CH_2{=}CHCHO$	$Ph_2POMe/TESCl$[d] (B)	100°, 1/2 h	(100)	< 1:99
5	$CH_3CH{=}CHCHO$	$TMSOP(OMe)_2$ (A)	55°, 18 h	90	75:25
6	$CH_3CH{=}CHCHO$	$(MeO)_3P/TMSCl$ (B)	55°, 3 h	62	> 99:1
7	$CH_3CH{=}CHCHO$	$TESOP(NMe_2)_2$ (A)	0°, 1/2 h[c]	95	> 99:1
8	$PhCH{=}CHCHO$	$TESOP(NMe_2)_2$ (A)	0°, 1/2 h[c]	93	> 99:1
9	 $CH_2{=}CH\overset{O}{\overset{\|}{C}}CH_3$	$TMSOP(OMe)_2$ (A)	50°, 6 h	88	< 1:99
10	 $CH_2{=}CH\overset{O}{\overset{\|}{C}}CH_3$	$(MeO)_3P/TESCl$ (B)	100°, 2 h	79	< 1:99
11	 $CH_2{=}CH\overset{O}{\overset{\|}{C}}CH_3$	$TESOP(NMe_2)_2$ (A)	0°, 1/2 h[c]	82	< 1:99
12	 $CH_2{=}CH\overset{O}{\overset{\|}{C}}CH_3$	$Ph_2POCH_3/TESCl$[d] (B)	100°, 1/2 h	(100)	< 1:99

[a] Except where noted the reactions were carried out in the absence of solvent. [b] Yields reported are of distilled adducts. Yields in parenthesis were determined by nmr. In such cases distillation resulted in decomposition. [c] The reaction was carried out 3 M in THF. [d] Available from Aldrich Chemical Company.

olefin geometry of the 1,4-adducts 8, R = H, Me (Entries 4, 9, 10, 12, Table), is exclusively *Z*, a possible consequence of the intervention of oxaphospholenes such as 10 and 11. Second, α,β-unsaturated ketones locked in a transoid geometry such as cyclohexenone fail to undergo *any* detectable 1,4-addition. Finally, we have prepared the known oxaphospholene 11 (R = Me)[11] and have demonstrated that it undergoes a rapid exothermic reaction with trimethylchlorosilane to give the *Z*-phosphonate 8 (R = Me, X = OMe) in quantitative yield.

In conclusion, through a judicious choice of the phosphorus reagent one may achieve high regioselectivity for either 1,2 or 1,4-addition to α,β-unsaturated aldehydes, and regiospecific 1,4-addition to methyl vinyl ketone and presumably to related enones. The general class of phosphorus-activated olefins 7 and 8 (Scheme I) should prove to be useful carbon nucleophiles upon metalation. These studies are now in progress.

Scheme II



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