Pergamon

Tetrahedron Letters 39 (1998) 7857–7860

TETRAHEDRON LETTERS

Stereo-controlled Synthesis of Styrylphosphines and their Oxides or Sulfides Using Phosphonium Diylides

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Received 29 April 1998; accepted 19 August 1998

Abstract : Lithium dimethyldiphenylphosphonium diylide reacts with electrophiles such as Ph_2PCl, $Ph_2P(O)Cl$ or $Ph_2P(S)Cl$ to give monoylide intermediates allowing by reaction with benzaldehyde the synthesis of the styrylphosphines or the corresponding oxides or sulfides. This efficient *one-pot* method permits at choice the selective synthesis of each isomer *Z* or *E* and corroborates further the isomeric identification of the styrylphosphines.

In our recent work, we have shown that diphenylphosphonium diylides are excellent tools in organic synthesis.[1] Indeed, these reagents, more reactive than the corresponding triphenylphosphonium monoylides, afford a general synthetic method for numerous α,β-unsaturated functions. In order to further enlarge the field of application of these diylides, we have begun to study their reactivity towards phosphorus electrophiles such as chlorodiphenylphosphine and its oxide or sulfide (scheme 1).

The results reported here show that the diphenyldimethylphosphonium diylide **1** (scheme 1) reacts instantaneously at room temperature with Ph_2PCl (X= represents an electronic doublet), yielding *in situ* a new monoylide intermediate **2a**. The latter is probably spontaneously converted into the new less non-stabilized monoylide **3a** *via* an intramolecular proton transfer. Indeed the phosphorus NMR spectrum indicates the presence of **3a** by two doublets with the same $^2J_{PP}$ coupling constant (table 1). At this stage, direct addition of benzaldehyde to the reaction mixture (scheme 1), leads to the quantitative formation of the two isomers of the styrylphosphine **4a** (scheme 2 : **A** ; step b. overall isolated yield : 95%). This last step, corresponding to a Wittig reaction is performed in very mild conditions (one minute at 20°C). According to the non-stabilized character of the monoylide **3a**, the major isomer is *Z*, separated from the *E* by classic column chromatography (*Z/E = 90/10*).

To our knowledge, four methods are reported in the literature for the synthesis of styrylphosphines, namely the reaction of lithium diphenylphosphide with phenylacetylene or β-bromostyrene,[2a] the reaction of diphenylphosphine with phenyl acetylene,[2b] the reaction of styryl Grignard with diphenylchlorophosphine,[2c] and a Horner reaction between benzaldehyde and a phosphinoxy carbanion.[2d] However, the problems encountered make these methods not totally satisfactory : In the first, the styrylphosphine could be isolated only as the corresponding oxide and in very low yields, in

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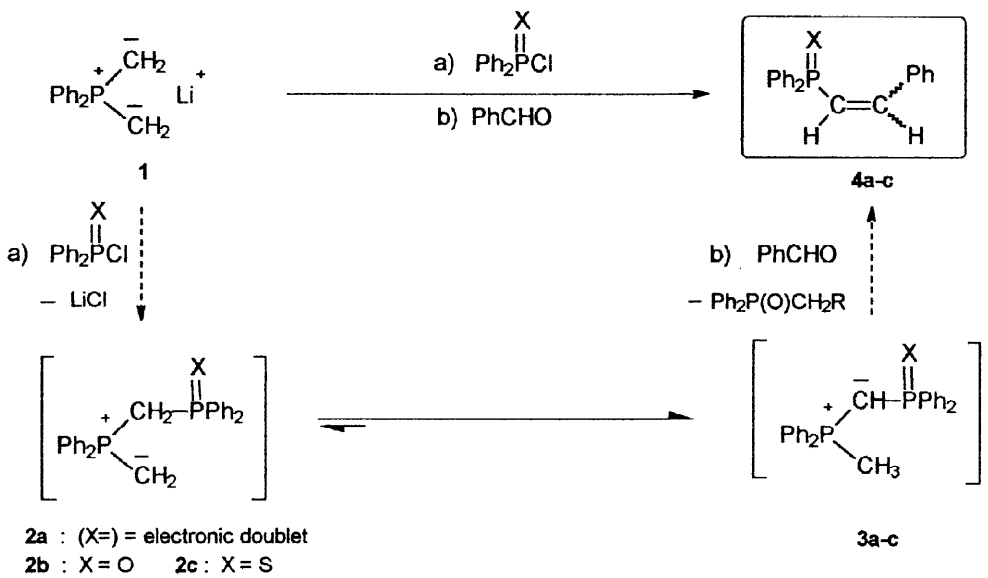
0040-4039/98/$ - see front matter
PII: S0040-4039(98)01758-4

the second one an UV-irradiation during a long time was necessary and, in the third, isomerization problems were encountered. Concerning the last one, a diphosphorus precursor of the phosphinoxy carbanion was previously isolated and nothing was said about the stereochemistry of the reaction. In comparison our method is interesting because it allows, thanks to the properties of the diphenyl dimethylphosphonium diylide **1**, an efficient *one-pot* stereoselective synthesis of the styrylphosphine *via* a Wittig reaction in the double bond formation step.



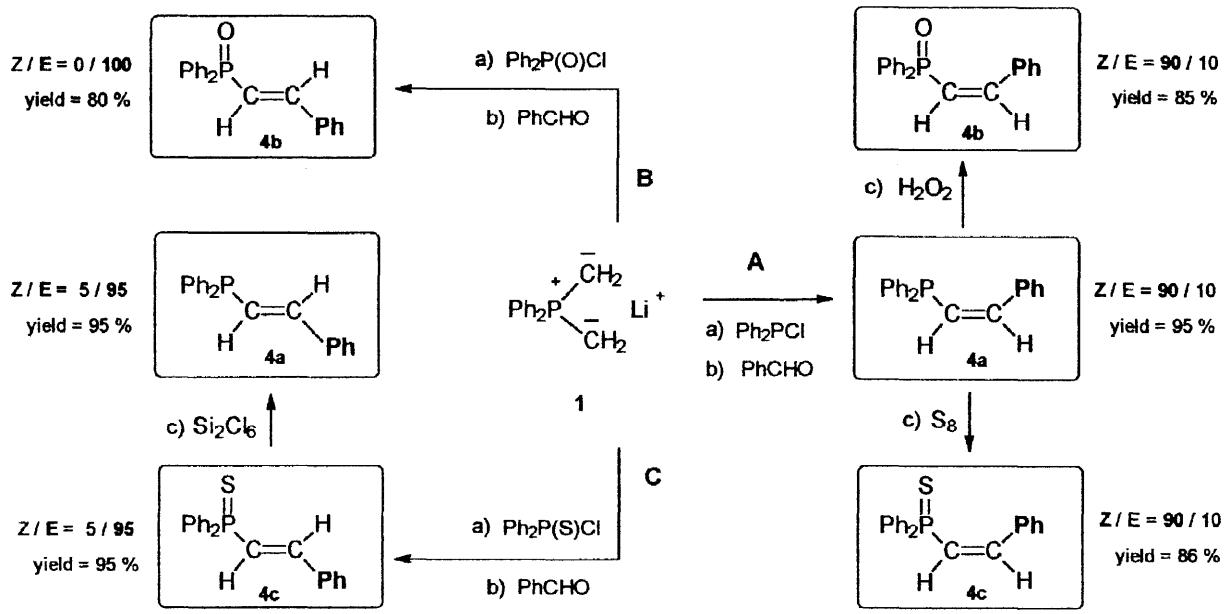
Scheme 1. Study of the reactivity of phosphonium diylides type **1** towards phosphorus electrophiles. Application to the synthesis of α,β-unsaturated phosphorus compounds.

We could generalize this new synthetic pathway, starting from $Ph_2P(O)Cl$ as electrophile. Thus the formation of **3b**, followed by the *in situ* addition of benzaldehyde leads through a Wittig reaction in the last step, to the synthesis of the corresponding styrylphosphine oxide **4b** (scheme 1 : X = O). The reaction, instantaneous and in very mild conditions, leads this time to the quantitative formation of the *E* isomer (scheme 2 : **B**). This result is consistent with an intermediate monoylide **3b**, substituted by the electron-withdrawing group $Ph_2P(O)$, and stabilized.[3] Finally, using $Ph_2P(S)Cl$ as electrophile, the corresponding styryl phosphine sulfide **4c** was synthesized rapidly in very good yield and exclusively in the *E* configuration (*E*/*Z* > 95/5), $Ph_2P(S)$ being also an electron-withdrawing group (scheme 2 : **C** ; step a and b).

We thought then that it would be interesting from a synthetic point of view to complete these results to develop a general method allowing the selective formation of the *E* or *Z* isomers of the styryl phosphine or the formation of their oxide and sulfide derivatives.

Thus, by *in situ* addition to the reaction mixture, containing the styryl phosphine **4a** (*Z*/*E* : *90/10*), of sulfur or hydrogen peroxide, we could obtain essentially the corresponding *Z* sulfide **4c** or oxide **4b**, no isomerization being observed during this last step (scheme 2 : A ; steps c). In addition, the synthesis of the last missing molecule, namely the *E*-styrylphosphine **4a**, was easily and stereospecifically achieved by the *in situ* reduction of the *E*-styrylphosphine sulfide **4c** with 1.5 equivalents of Si_2Cl_6 (scheme 2 : **C**

; step c). Notice that in this last case the exchange of THF by toluene as reaction solvent gives cleaner results. From the synthetic point of view, all the isomers **4a-c** were isolated in very good yields by classical work-up, a treatment with NaOH being however necessary in order to eliminate the hexachlorodisilathiane $S_2Si_2Cl_6$ formed during the reduction of the P=S bond.



Scheme 2. *Stereo-contolled synthesis of styrylphosphines and their oxides or sulfides.*(i) The indicated yields correspond to isolated products (*E* + *Z*). (ii) *Z*/*E* is determined by ^{31}P and ^{1}H NMR. (iii) Formation rate of 4a, 4b or 4c in each step of the scheme : 100% (determined by ^{31}P NMR). (iv) When there is an isomer mixture their separation is easily performed by column chromatography. (v) Whatever pathways **A**, **B** or **C**, all the steps described in the scheme are realized in mild conditions (1 mn at 20°C).

Concerning the two isomers of the styrylphosphine **4a**, an interesting exception to the classical Karplus-type relationship about the coupling constants $^{3}J_{HH}$ of the double bond is noteworthy. Indeed, the comparison with the literature shows that for the styrylphosphine this constant is higher for the *Z* isomer than for the *E* one.[2c, 4] Another phenomenon is the surprising shielding of the signal corresponding to the *Z* isomer in ^{31}P NMR, which can be explained by the presence of a steric compression between the phenyl of the styryl moiety and the free doublet of the phosphorus atom.[2c]

However the earlier assignment of the ^{31}P chemical shifts and the $^{3}J_{HH}$ coupling constants to the correct *E* or *Z* styrylphosphine is not totally unambiguous. Indeed, in the literature this identification is based on a synthetic method, namely the reaction of Ph_2PCl with the Grignard reagent of the *Z* or *E* bromostyrene, which affords a mixture of the two isomers of the styrylphosphine.[2c] Moreover, we have to be careful in the isomeric attribution because the inversion of the $^{3}J_{HH}$ is not clearly linked to the geometry of the molecule. For example no apparent inversion is seen when the phenyl of the styryl group is replaced by a *tertio*-butyl group.[4]

However, our results seem to confirm the identification given in the literature. Indeed, as we have already mentionned our direct synthesis of the styrylphosphine **4a** from Ph_2PCl offers the *Z* isomer as the major product, because of the non-stabilized character of the intermediate Wittig reagent **3a**.

Taking this into account, the comparison of the $^3J_{HH}$ constants confirms that the *cis* $^3J_{HH}$ of the *Z* isomer is larger than the *trans* $^3J_{HH}$ of the *E* one. Moreover, the reduction with Si_2Cl_6 of the well identified *E* styrylphosphine sulfide **4c** (scheme 2 : **C** ; step c), gives a molecule showing spectra corresponding exactly to those attributed to the *E* styrylphosphine **4a**, obtained directly as the minor isomer from Ph_2PCl (scheme 2 : **A** ; step a and b). Notice for this last case that the reaction in work-up conditions does not give stereoisomerization at all.

Table 1. Characteristic data [δ ^{31}P (ppm), δ ^{1}H (ppm) and *J* (Hz)][a] for the styrylphosphines **4a** and their corresponding oxides **4b** and sulfides **4c**, and for the Wittig monoylide intermediates **3a**, **3b** and **3c**.[b]

compound		δ P	$^2J_{PP}$	$^3J_{PC}$	δ H_{PCH}	$^2J_{PH}$	δ H_{PCCH}	$^3J_{HH}$
4a	*Z*	-24.2		2.27[c]	6.47	2.77	-[e]	12.65
4a	*E*	-10.8		9.76[d]	7.18	0	-[e]	10.83
3a		15.9 and -20.2[f]	158.76					
4b	*Z*	20		7.3	6.32	19.5	7.54[g,h]	14.08
4b	*E*	25.47		17.9	6.83	22.3	7.6	17.37
3b		29.7 and 13.7[f]	21.49					
4c	*Z*	29.36		6.84	6.41	17.89	-[e]	13.61
4c	*E*	37.76		19.3	6.96	21.18	7.61	16.66
3c		34.9 and 15.5[f]	30.12					

(a) Solvent : $CDCl_3$. (b) All isomers *Z* and *E* for **4a-c** are fully characterized (c) Literature : 0 Hz. (d) Literature : 17.4 Hz ($CDCl_3$). (e) Hidden. (f) Solvent : THF. (g) $^3J_{PH}$ = 54 Hz. (h) Literature : 7.97 ppm ($CDCl_3$).

Further evidences for the interaction of the lone pair of the phosphine is that the inversion of the $^3J_{HH}$ and the shielding in $\delta(^{31}P)$ in the case of the *Z* styrylphosphine, respectively disappears and diminishes for the corresponding oxide and sulfide.

We have developed a general, stereoselective and new synthetic method for styrylphosphines and for their corresponding oxides and sulfides. This efficient *one-pot* pathway, probably generalizable to other α,β-unsaturated phosphines and phosphorus compounds, shows once again the general interest of phosphonium diylides in organic synthesis.

Acknowledgement. We thank P. Beuchet and S. Scheinz for their contribution to this work.

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