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OPTICALLY ACTIVE PHOSPHINES : NEW SYNTHETIC APPROACH

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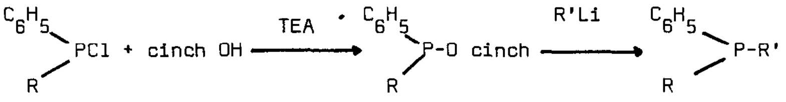
Three general methods of access to optically active phosphines, including a classical separation of diastereoisomers, are known. Two of them, often used, are indirect methods.

- The synthesis described by HORNER (1) involves a separation of quaternary phosphonium salts.
- The MISLOW procedure, implying a separation of menthyl P(IV) esters (2), first provides phosphine oxides, which are reduced by Si_2Cl_6.
- The third one, especially appreciable, leads to optically enriched products (3).
- Recently, MIKOLAJCZYK reported that the principle of asymmetrical induction could be applied to the synthesis of methyl ethylphenylphosphinite, whose condensation with methyllithium provides the corresponding optically active phosphine with "stereospecific inversion" (4).
- Various synthetical aspects have been recently summarized (5).

We wish to report here our most significant results concerning the condensation of cinchonine (cinch OH) with several arylchlorophosphines (6). The substitution of the cinchonine group of the resulting ester by organolithium compounds leads to optically active phosphines.



The reactions are extremely simple to carry out whatever the molar fraction may be.

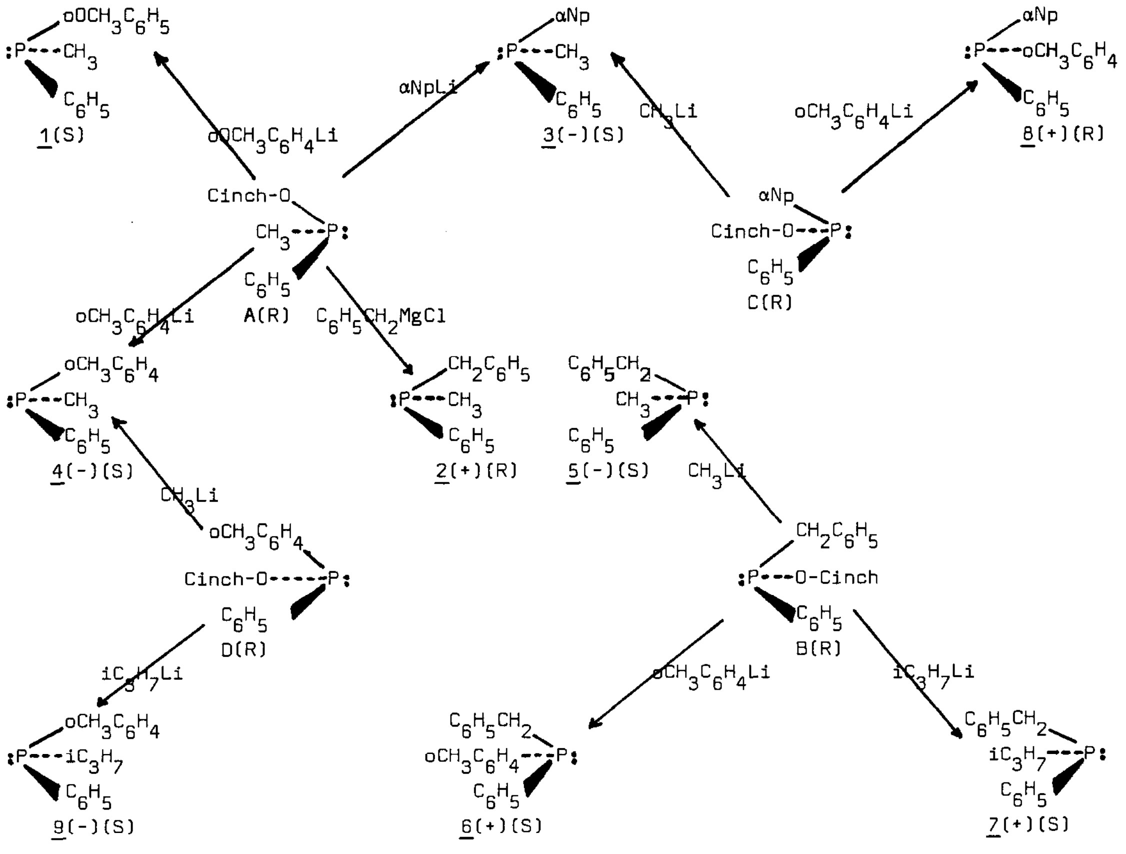
The first step consists of the introduction of a very slight excess of chlorophosphine into a THF suspension of cinchonine, which results in a rapid formation of a soluble complex. The substitution of chlorine is generally complete in a few hours at room temperature, after addition of an equivalent of triethylamine. Purification of the intermediate phosphinite, essential for the second substitution, can be achieved by simple water washing (7).

The ester is treated with a moderate excess of R'Li(for a few hours at 0°C). Cinchonine is eliminated by an efficient acid washing (7). After evaporation of the organic layer, the resulting phosphines are usually of high purity when both substitutions are achieved in anhydrous and strictly non-oxidising media.

In these conditions, both substitutions are fairly quantitative, except in the case of $oOCH_3C_6H_4Li$ (8) for which the yield does not exceed 75 %, possibly because of the quaternization due to the bromobutane present. When non volatile byproducts are formed (e.g. in the last case), the phosphine is purified by "adsorption" on cuprous cyanide in moderate excess.

Besides, stoichiometrical complexes of phosphine and cuprous iodide, very amenable storage intermediates, can be easily tested by physical methods owing to their solubility (9).

Transformation of the phosphines into phosphine oxides, in benzenic solution by diluted H_2O_2 at 5°C, allows us to establish a correlation scheme and to determine the optical purity (see table).



TABLE

N°	R	R'	$\alpha_D^{CHCl_3}$ phosphine	$\alpha_D^{CHCl_3}$ phosph. oxide	estimated optical purity %
1	CH_3	o.$(OCH_3)C_6H_4$	+ 4**	+ 16°,1*	62
2	CH_3	$C_6H_5CH_2$	+ 19	- 9*	18
3	CH_3	αNp	- 40	- 1,9	62
4	CH_3	o.$CH_3C_6H_4$	- 2	+ 16,5	62
5	C_6H_5-CH_2	CH_3	- 20,2	+ 10*	20
6	C_6H_5-CH_2	o.$CH_3C_6H_4$	+ 27,4	+ 29,8	20
7	C_6H_5-CH_2	iC_3H_7	+ 31,2	+ 8	20
3	αNp	CH_3	- 52	- 3,2	80
8	αNp	o.$CH_3C_6H_4$	+ 17,2	- 8	80
4	o.CH_3-C_6H_4	CH_3	- 1,2	+ 10,5	39
9	o.CH_3-C_6H_4	i.C_3H_7	- 3,1	+ 17	39

*CH_3OH αNp = αNaphtyl ** cuprous iodide complex

To obtain this correlation, we consider two phosphine oxides of relatively high rotation, whose configurations have been established.

R = CH_3 R' = C_6H_5-CH_2 (R) αD_{CH_3OH} = + 51° (2)
R = CH_3 R' = o.$OCH_3C_6H_4$ (R) αD_{CH_3OH} = + 25°,9 (10)

We can therefore determine the absolute configuration of the 1, 2 and 5 phosphines and their optical purity, together with the (R) configuration of the major esters A and B.

The (R) configuration of the major esters C and D results directly from the same principle of inversion in the substitution by organolithium compounds. The optical purities are calculated on the assumption that all substitutions by lithium derivatives are realized with the same degree of stereoselectivity (11).

For the moment, it seems rather premature to estimate the exact stereoselectivity of these substitutions. However, these optical purities can be considered as the basis of an approximate estimation of the diastereoisomeric esters ratios (12) (estimation based on the highest rotation of phosphine or corresponding phosphine oxide), which varies with R.

R = $C_6H_5CH_2$: 60/40 R = CH_3 : 81/19
R = αNp : 90/10 R = o.$CH_3C_6H_4$: 70/30

The difference in steric requirements between the two organic groups on the phosphorus atom seems to be the main factor.

At this stage, it is difficult to say whether the stereochemistry of the intermediate ester is thermodynamically or kinetically controlled. However, we have some evidence in other series for a kinetic factor (13).

Acknowledgements

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References :

1. L. HORNER, H. WINKLER, A. RAPP, A. MENTUP, H. HOFFMANN und P. BECK
Tetrahedron Letters n° 5 p. 161-166 (1961).
2. Olaf KORPIUM, Robert A. LEWIS, James CHICHOS and Kurt MISLOW
J. Am. Chem. Soc. 90, 4842 (1968) and references therein
3. K. TANI, Leo D. BROWN, JAMIL Ahmed, James A. IBERS, M. YOKOTA,
A. NAKAMURA and S. OTSUKA
J. Am. Chem. Soc. 99, 7876 (1977)
4. Jan OMELANCZUK and Marian MIKOLAJCZYK
J.C.S. Chem. Comm. 1976, 1025.
5. TANAKA-MASATO, Yuki GOSEI KAGAKU KYOKAISHI 1978, 36(1) 41-8.
6. D. JORE, D. GUILLERM et W. CHODKIEWICZ
J. Organomet. Chem. 147, C_7 - C_9 (1978)
7. For these purposes it seems necessary to add previously, to the organic solution, one volume of ether and three volumes of pentane. In the first step, addition of a second equivalent of TEA is advisable.
8. Robert A. LEWIS and Kurt MISLOW
J. Am. Chem. Soc. 91, 7009 (1969).
9. The free phosphine can be immediately recovered by an alkalicyanide treatment.
10. B.D. VINEYARD, V.S. KNOWLES, M.J. SABACKY, G.L. BACHMAN and D.J. WEINKAUFF
J. Am. Chem. Soc. 99 - 5946 (1977).
11. Electropositivity of the metal enhances the stereoselectivity, which is considerably lower with benzyl Grignard derivative.
12. These esters are now being investigated.
13. Unpublished results of our laboratory.

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