

STERESELECTIVE SYNTHESIS OF PHOSPHINITE COMPLEXES
 NEW ROUTE TO CHIRAL PHOSPHINES

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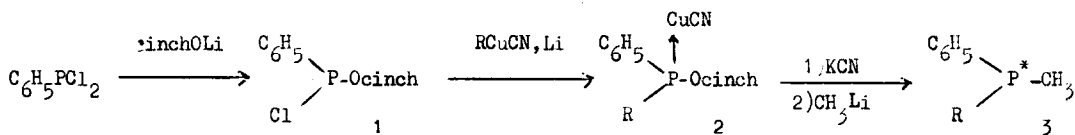
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SUMMARY

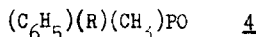
Consecutive substitutions of chlorine in dichlorophenylphosphine by lithium cinchoninate and arylcyanocuprates lead stereoselectively to the corresponding (R) P^{III} esters; the latter are converted, by methyl lithium, into chiral phosphines.

Several methods of access to optically active phosphines have been elaborated (1). Recently we described the synthesis of chiral phosphines from dissymmetrical chlorophosphines (2).

We wish to report here our first results concerning a direct synthesis of such phosphines from dichlorophenylphosphine:



A slow introduction at low temperature (-73°C) of lithium cinchoninate (3) into a toluene solution of dichlorophenylphosphine leads to the intermediate chloroester 1, which is directly transformed into 2 by addition of an equivalent of arylcyanocuprate (4) - also at low temperature. After hydrolysis, a highly insoluble complex is isolated with a quantitative yield. Different phosphinite complexes are transformed into phosphines 3 by potassium cyanide treatment followed by condensation with methyl lithium. These phosphines are oxidised to the corresponding oxides 4 in benzene solution by dilute H₂O₂.



| R | Yield (a)% | [α] _D methanol | Enantiomeric excess | Reference phosphine oxides | | |
|--|------------|---------------------------|---------------------|----------------------------|---------------------------|-----------------------------|
| | | | | Ref. | [α] _D methanol | Chirality at P [*] |
| <u>o</u> -CH ₃ OC ₆ H ₄ | 60 (b) | + 13,6° | 52 % | (6) | + 25,9° | <u>R</u> |
| <u>o</u> -CH ₃ C ₆ H ₄ | 60 (b) | + 22° (d) | 68 % | (2b) | + 31,8°(d) | <u>R</u> |
| <u>p</u> -CH ₃ OC ₆ H ₄ | 40 (c) | + 6,2° | 77 % | (1b) | - 8° | <u>S</u> |
| <u>p</u> -CH ₃ C ₆ H ₄ | 45 (c) | + 14,5° | | (5) | - 8,6° | <u>S</u> |

a) Based on C₆H₅PCl₂

b) Crude, treated with pentane, pure by NMR

c) Purified d) Chloroform

Ortho-substituted arylcuprates lead to better yields than the para-substituted ones which are presumably more reactive towards the chloroester 1 and less selective. Substitution by CH_2Li has been estimated to be quantitative (2) therefore the percentage of 2 in the raw complex should correspond to the above yields (7).

The methylphenyl o-tolylphosphine oxide has also been prepared from 1 by addition of an equivalent of dimethylcuprate, substitution by o-tolyl lithium and oxidation. Specific rotation $[\alpha]_{\text{D}}^20 \text{CHCl}_3 = -8^\circ$ indicates S configuration (at phosphorus) as predominant in the ester. We can therefore assume that the stereochemistry of the second step is the same whatever the entering group may be and that all major esters 2 (R = aryl) are of configuration R.

The diastereoisomeric ratio in 2 is directly correlated with EE value (2)(8)(9). The relatively high stereoselectivity of the second step of the reaction could a priori be explained by three different hypotheses :

- 1) Equilibration, in the reaction medium, of diastereoisomers 2. This hypothesis is to be discarded: several attempts of equilibration of enriched minor ester 2 (R = o- $\text{CH}_2\text{C}_6\text{H}_4$) have been unsuccessful.
- 2) The ratio of diastereoisomers 2 reflects the stereoisomerism in the intermediate chloroester 1. This is also unlikely because of the variation of this ratio with the group R.
- 3) Different reactivities of diastereoisomeric chloroesters in equilibrium (10).

The above results would not justify a detailed discussion of this hypothesis ; our next paper is essentially devoted to this problem.

Phosphines of fairly high optical purity can be rapidly prepared by this method ; a one-pot synthesis can be achieved if the final substitution is done on the complexed ester (2b). Furthermore major esters may be purified by crystallisation (2b).

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 b) O. KORPIUM, R.A. LEWIS, J. CHICKOS & K. MISLOW J. Am. Chem. Soc. 90, 4842, (1968) & ref. therein
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- (2) a) W. CHODKIEWICZ, D. JORE & W. WODZKI Tetrahedron Letters 1069, (1979)
 b) W. CHODKIEWICZ, D. JORE, A. PIERRAT & W. WODZKI J. Organomet. Chem. (in press)
- (3) a) Lithium cinchoninate is prepared by progressive introduction of CH_2Li into a THF suspension of cinchonine (1 mole/l). Dissolution of cinchonine and subsequent brown coloration are used as indicators of the complete metallation.
 b) Other condensation systems such as cinchonine - triethylamine or magnesium cinchoninate are less efficient.
- (4) These reagents are prepared at -10°C in a 1/1 ether/THF solution : H. GILMAN, R.G. JONES, L.A. WOODS J. Org. Chem. 17, 1650, (1952)
- (5) R.D. BAECHLER & K. MISLOW J. Am. Chem. Soc. 92, 3090, (1970)
- (6) B.D. VINEYARD, V.S. KNOWLES, M.J. SABACKY, G.L. BACHMAN & D.J. WEINKAUFF J. Am. Chem. Soc. 99, 5946, (1977)
- (7) The second step is never complete : it seems therefore likely that an "anhydride type" by-product of hydrolysis would lead to certain amounts of dimethylphenylphosphine. The corresponding oxide is generally eliminated by water washing.
- (8) Complexes 2 are easily transformed into the corresponding phosphinates whose diastereoisomerism can be estimated by NMR (unpublished results).
- (9) J. OMELANCZUK & M. MIKOLAJCZYK J.C.S. Chem. Com., 1025, (1976)
- (10) A rapid equilibrium has been suggested for a similar trivalent phosphorus compound : B. FONTAL & H. GOLDWHITE Tetrahedron, 22, 3275, (1966)

(Received in UK 6 July 1979)