The Palladium-catalysed Reaction of Lithium Diphenylthiophosphides with Allylic Carboxylates. A Stereoselective Synthesis of Phosphine Sulphides

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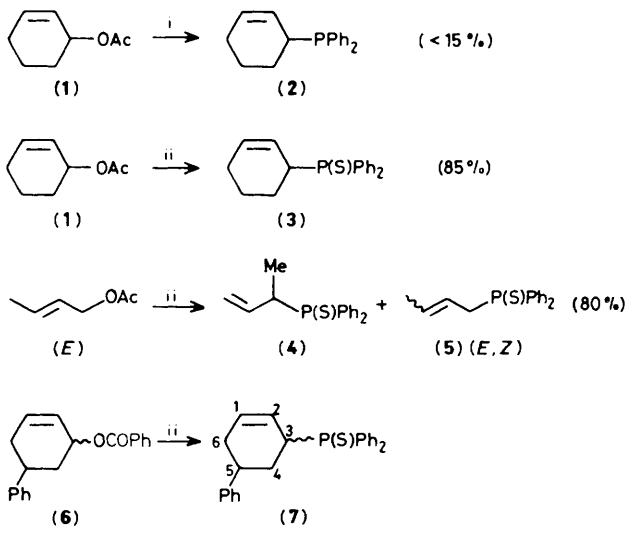
The palladium-catalysed substitution of allylic carboxylates with lithium diphenylthiophosphides takes place with overall retention of configuration, leading to allylic diphenylphosphine sulphides in high yield.

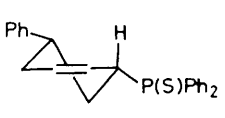
A Pd-catalysed reaction leading to C–P bond formation has recently been described producing vinyl, aryl, and allyl phosphonates from reactions of $HP(O)(OR)_2$ with alkenyl bromides and 1,3-dienes.[1] In conjunction with our interest in extending the range of active nucleophiles in the Pd-catalysed substitution of allylic acetates[2] and to determine the applicability of this reaction in forming C–P bonds, we have investigated phosphorus nucleophiles, such as phosphides and thiophosphides. We report here a ready and stereoselective method for preparing allylic phosphine sulphides from allylic carboxylates *via* a Pd-catalysed reaction.



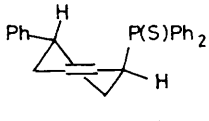
Reagents: i, $LiPPh_2$, 5 mol% $Pd(PPh_3)_4$, THF, room temp.; ii, $LiP(S)Ph_2$, 5 mol% $Pd(PPh_3)_4$, THF, room temp.

The reaction of $LiPPh_2$ with cyclohex-2-enyl acetate (**1**) in the presence of 5 mol% of $Pd(PPh_3)_4$ gave, even in refluxing tetrahydrofuran (THF), only limited yields (<15%) of (**2**), owing to the co-ordinating properties of the phosphine produced which deactivates the catalyst. In contrast, lithium diphenylthiophosphide[3] reacted with (**1**) at room temperature to give (**3**) in high yields. Under similar conditions, (*E*)-but-2-enyl acetate yielded a 67:25:8 mixture of the thiophosphines (**4**), *E*-(**5**), and *Z*-(**5**), with partial scrambling of the regio- and stereo-chemistry of the allylic group; rather unexpectedly, the branched isomer predominated.

The stereochemistry of the Pd-catalysed reaction was investigated using the 5-phenylcyclohex-2-enyl system. The reaction of *cis*-(**6**)[4] with lithium diphenylthiophosphide yielded *cis*-(**7**) as a single diastereoisomer, whereas reaction of an 83:17 (by h.p.l.c.) *trans–cis*-mixture of (**6**)[5] gave *trans*-(**7**) as the major product (contaminated with 18% of the *cis*-isomer). The ^{13}C signals and ^{31}P–^{13}C couplings for C-3 to C-6 were assigned from the examination of the ^{13}C n.m.r. spectra at two different frequencies (15.08 and 62.86 MHz) and by comparison with available parameters for one- and two-bond couplings.[6]† The Karplus-like dependence of vicinal ^{31}P–^{13}C coupling on



cis - (**7**)



trans - (**7**)

† ^{13}C-{^1H} N.m.r. data ($CDCl_3$;Me_4Si), δ in p.p.m. (J_{CP} in Hz); *cis*-(**7**): C-3, 39.96 (56.7); C-4, 33.56 (2.7); C-5, 40.14 (12.9); C-6, 29.34; *trans*-(**7**): C-3, 36.85 (53.1); C-4, 31.02 (3.7); C-5, 35.37 (3.7); C-6, 29.81; (**3**) C-3, 38.46 (55.8); C-4, 24.67 (2.7); C-5, 21.33 (10.1); C-6, 22.46.

the dihedral angle has been established for the $Me_2P(S)$ group.[7] The stereochemistry of the diastereoisomers could be unambiguously assigned if one assumes similar couplings for the $Ph_2P(S)$ function; a 12.9 Hz value for $^3J(^{31}P-^{13}C\text{-}5)$ reflected a dihedral angle of *ca.* 180° and indicated a pseudo-equatorial position for the $-P(S)Ph_2$ group, in a half-chair conformation. In contrast, a 3.7 Hz value for $^3J(^{31}P-^{13}C\text{-}5)$ in the other isomer revealed a pseudo-axial orientation for this group; in this isomer severe 1,3-diaxial strain would rule out an axial position for the Ph-group and identified it as being the *trans*-isomer. Consequently, the former isomer is *cis*.

These stereochemical assignments indicate that the substitution of the carboxylate group for $P(S)Ph_2$ was quite selective with overall retention of configuration at carbon according to a Trost-type mechanism.[8] The observed stereoselectivity shows that the phosphorus atom of the reagent (diphenylthiophosphido anion) attacks the face of the η^3 allylic ligand opposite to palladium. The reduction of the sulphide (**3**) to the phosphine (**2**) could be achieved by a classical procedure,[9] *e.g.* sodium in toluene.

This method for the synthesis of phosphine sulphides from readily available allyl carboxylates with retention of the configuration at the carboxylate-bearing carbon atom could complement the procedure from allylic tosylates, the stereochemistry of which has not yet been established.

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