

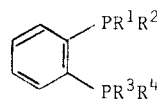
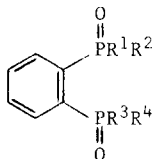
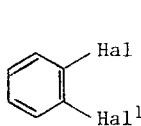
A NOVEL SYNTHESIS OF o-DIPHOSPHORYLBENZENES

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Abstract: Synthesis of phosphorylchloroacetylenes, diphosphorylacetylenes and the Diels-Alder reactions of the latter to produce o-diphosphorylbenzenes are described.

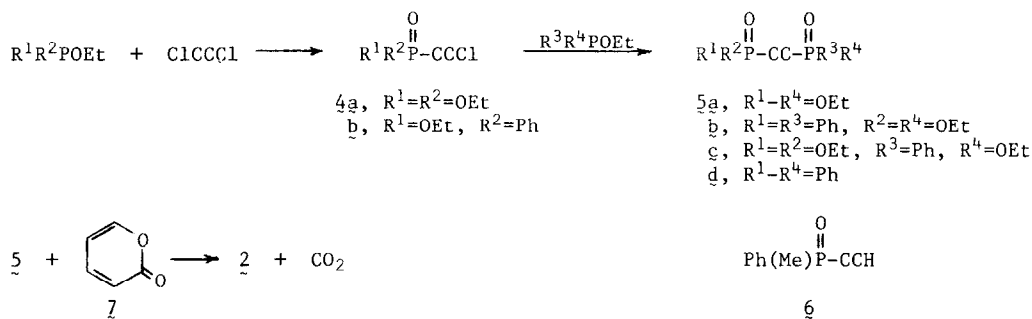
We have been interested for some time in the synthesis of o-diphosphoryl species of the type 2 as precursors to o-diphosphines (3) which can serve as ligands for transition metals. Of particular interest to us are 2 ( $R^2=R^4=OR$ ) which can be reduced to species containing at least one P-H bond on each phosphorus atom (i.e. 3,  $R^2=R^4=H$ ), since these can then be incorporated into macrocyclic ligands.<sup>1</sup> The o-dihalogen precursor has been transformed into 2 via



a transition metal-catalyzed Arbusov reaction (poor yield)<sup>2</sup> or by photoactivated processes ( $R^1-R^4=OMe^3$  or  $R^1-R^4=OEt^4$ ) in better yields. The photoactivated substitutions have drawbacks in that in the former case the relatively inaccessible 1 ( $Hal=I, Hal^1=Br$ ) must be used,<sup>3</sup> and in the latter, with the more accessible 1 ( $Hal=I, Hal^1=Cl$ ), the photolysis must be carried out in liquid ammonia in dilute solution.<sup>4</sup> To our knowledge, no unsymmetrical species 2 ( $R^1 \neq R^3, R^2 \neq R^4$ ) have been synthesized. The reduced 3 can be formed directly from 1, but with one

exception, where  $R^1-R^4=NEt_2$ ,<sup>5</sup> all compounds synthesized via this route have been o-bis-(tertiaryphosphino)benzenes (3,  $R^1-R^4=alkyl$  and/or aryl).<sup>6</sup>

We now report a route to 2 which appears to be flexible enough to allow considerable variation in the types of substitution at the o-phosphorus atoms, and circumvents substitution reactions of rather stable aromatic carbon-halogen bonds. Reaction of 5a-d and  $\alpha$ -pyrone (7)<sup>7</sup> in o-dichlorobenzene at 180°C for 3-4 h followed by chromatography on silica gel (EtOAc) gave the corresponding aromatized Diels-Alder products 2 in isolated yields of 60-70%.<sup>8</sup> Only a single activating group on the alkyne is necessary for the cycloaddition to occur, as 6 reacted as readily as the diactivated 5. On the other hand, bis(diphenylphosphino)acetylene ( $Ph_2PCCPPh_2$ ) failed to react with 7 under a variety of conditions, including Lewis acid catalysis.



The Diels-Alder reaction is relatively straightforward. The important feature in this approach is the synthesis of the appropriate alkyne dienophiles. Reaction of dichloroacetylene<sup>9</sup> in diethyl ether at -20°C with a trivalent phosphorus species containing at least one P-OEt bond allows the isolation of 4 in high yield (e.g. 4a; 90% distilled).<sup>10</sup> This allows the synthesis of unsymmetrical species, of which 5c (55% yield) is an example. Species 5a and 5b were obtained in one pot reactions (reaction at -15°C, 2 h, followed by 40°C, 1 h) in yields of 45 and 34%, respectively. Although it is less convenient, higher yields are obtained if 4 is purified and then carried on to 5: this procedure gave 5a and 5b in 86 and 70%, respectively. The Table summarizes yields and <sup>31</sup>P NMR chemical shifts of 5 and 2.

We should add also that the above approach to the phosphoryl alkynes involves phosphorus nucleophiles and alkyne electrophiles. It is conceivable that nucleophilic alkynes (Grignards,

Table. Yields and  $^{31}\text{P}$  NMR data for the diphosphoryl alkynes 5 and Diels-Alder adducts 2.<sup>a,b</sup>

|           | <u>Yield</u> | $^{31}\text{P}$ NMR<br><u><math>\delta</math> (ppm)</u> |           | <u>Yield</u> | $^{31}\text{P}$ NMR<br><u><math>\delta</math> (ppm)</u> |
|-----------|--------------|---|-----------|--------------|---|
| <u>5a</u> | 86           | -10.4   | <u>2a</u> | 72           | 15.4  |
| <u>5b</u> | 50           | 7.1, 7.0 <sup>d</sup>                                   | <u>2b</u> | 70           | 31.9, 30.4 <sup>d</sup>                                 |
| <u>5c</u> | 54           | 7.2, -10.3 <sup>e</sup>                                 | <u>2c</u> | 60           | 30.3, 15.6 <sup>e</sup>                                 |
| <u>5d</u> | <u>c</u>     | 8.9   | <u>2d</u> | 60           | 31.2  |

<sup>a</sup> Yields given are for isolated, purified materials.  $\text{R}^1\text{-R}^4$  for 2 are as defined for 5.

<sup>b</sup>  $^{31}\text{P}$  NMR chemical shifts downfield from 85%  $\text{H}_3\text{PO}_4$  (external standard) are defined as positive. Spectra were obtained on 0.2 M  $\text{CDCl}_3$  solutions.

<sup>c</sup> Obtained in quantitative yield by  $\text{H}_2\text{O}_2$  oxidation of commercially available  $\text{Ph}_2\text{PCCPPPh}_2$ .

<sup>d</sup> Each signal is a singlet: due to meso and dl diastereomers.

<sup>e</sup>  $J_{\text{P}_1\text{P}_2} = 11.1$  hz, each signal a doublet.

lithium reagents) and electrophilic phosphorus species (e.g. phosphoryl chlorides) could be used. We have devoted considerable effort to the development of the latter approach, and can say unequivocally that the Arbuzov method described above is far superior.<sup>11</sup>

To illustrate the utility of this synthetic approach we have recently reduced 2a to 3a ( $\text{R}^1\text{-R}^4=\text{H}$ ) in 50% yield using LAH in THF, and then incorporated this moiety into bis(secondary-phosphino)macrocycles.<sup>12</sup>

We are currently investigating more convenient dienes as well as nucleophiles other than phosphorus for the dienophile synthesis.

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#### References and Notes.

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9. Wotiz, J.H.; Huba, F.; Vendley, R. *J. Org. Chem.* 1961, 26, 1626.
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11. For example, 5b was synthesized in 8% overall yield in two steps:  $\text{HCCMgBr} + \text{Ph}(\text{MeO})\text{P}(\text{O})\text{Cl}(\underline{7}) \longrightarrow \text{Ph}(\text{MeO})\text{P}(\text{O})\text{CCH}(\underline{8}, 48\%); \underline{8} + \text{LDA} \xrightarrow{\underline{2}} \underline{5b}(17\%)$ . These reactions required extremely careful monitoring of reaction temperature and concentrations of reagents.
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