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# On the cycloaddition of arylphosphine oxides with dimethyl acetylenedicarboxylate

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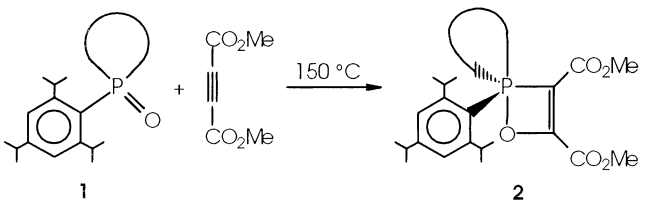
**Abstract**—The [2+2] cycloaddition reaction of dimethyl acetylenedicarboxylate (DMAD) and the P=O moiety of cyclic P-(2,4,6-triisopropylphenyl) phosphine oxides giving an entry to oxaphosphetes is of general value and extended to cyclic and alicyclic phosphine oxides with different trialkylphenyl substituents on the phosphorus atom. The structures of the products obtained by the [2+2] cycloaddition have been studied by semiempirical quantum chemical calculations 

We have found that the reaction of a series of P-(2,4,6-triisopropylphenyl) cyclic phosphine oxides (**1**) with DMAD leads to spirocyclic oxaphosphetes (**2**) that are the unsaturated derivatives of the oxaphosphetanes, well-known intermediates of the Wittig reaction (Scheme 1).[1,2]

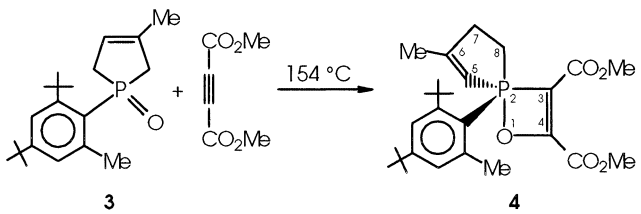
This is the first case that the P=O group of phosphine oxides was observed to take part in a [2+2] cycloaddition reaction.

In this paper, the [2+2] cycloaddition reaction is extended to other P-(2,4,6-trialkylphenyl) model compounds. The di-*tert*-butyl-methylphenyl- and the trimethylphenyl P-heterocycles (**3**,[3] **5**[4] and **7**[5]) synthesised in our laboratory served as excellent starting materials for the cycloadditions. The reaction of aryl-2,5-dihydro-1*H*-phosphole oxide **3** and 2,3,4,5-tetrahydro derivative **5** with DMAD at 154°C afforded the corresponding cycloadducts (**4**[6] and **6**,[7] respectively) in ca. 40% yield after column chromatography (Schemes 2



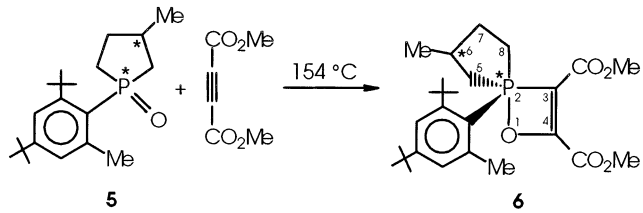

1 2

**Scheme 1.**




3 4

**Scheme 2.**




5 6

**Scheme 3.**

*Keywords*: phosphorus heterocycles; phosphine oxides; cycloaddition; theoretical studies.

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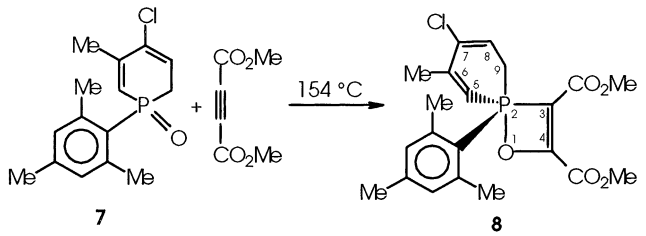
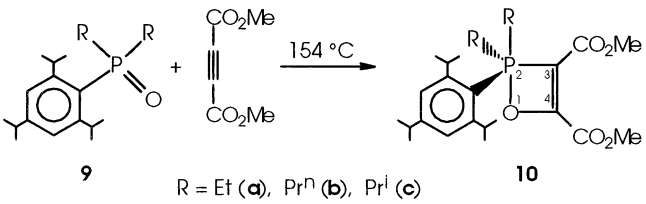
and 3). Due to the increased steric hindrance around the phosphorus atom, completion of the cycloaddition required prolonged reaction times (14 days). Product **6** was obtained as a 58:42% mixture of two diastereomers. Aryl-1,2-dihydrophosphinine oxide **7** also entered into an efficient cycloaddition with DMAD to give oxaphosphete **8**[8] (Scheme 4). All new products (**4**, **6** and **8**) were characterised by $^{31}P$ and $^{13}C$ NMR, as well as by IR and mass spectroscopic data. The $^{13}C$ NMR assignments were confirmed by spectra obtained by the Attached Proton Test technique. The pentavalent pentacoordinated state of the central phosphorus atom in compounds **4**, **6** and **8** has been proved by the four $^{1}J_{PC}$ couplings (57.9–107.7 Hz). The $^{13}C$ NMR spectral parameters were similar to those reported for the analogous triisopropylphenyl derivatives (**2**).[2] The IR spectrum also supported the oxaphosphete structure, as the intensive peak at 757 $cm^{-1}$ must be due to the symmetric P–O–C stretching vibration. The weak, but significant absorption at around 1670 $cm^{-1}$ that is a characteristic stretching vibration for tetrasubstituted ethylenes, was also convincing.

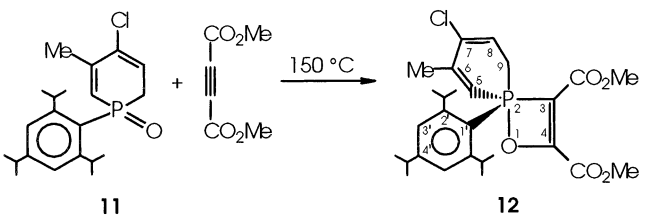
We wished to test if the [2+2] cycloaddition also works with alicyclic trialkylphenylphosphine oxides. It was found that the cycloaddition also took place with dialkyl-triisopropylphenyl phosphine oxides **9a** and **9b**,[9] although with much poorer outcome. The resulting oxaphosphetes (**10a**[10] and **10b**,[11] respectively) are the first examples of this kind of products that are not spirocyclic (Scheme 5). It is probably due to the increased steric hindrance that the diisopropylphosphine oxide **9c** could not be involved in a cycloaddition reaction.




**Scheme 4.**




**Scheme 5.**

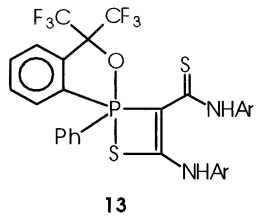


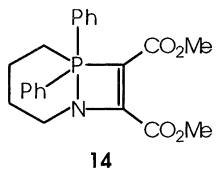

**Scheme 6** (Ref. 2).

The geometry of oxaphosphete **12**, that was formed in the reaction of dihydrophosphinine oxide **11** with DMAD, instead of the originally expected Diels–Alder cycloadduct (Scheme 6),[2] was evaluated by PM3 semiempirical calculations[12] that are especially well suited for computation of organophosphorus compounds.[13,14] The fully optimised structure of **12** is shown in Fig. 1,[15] while a selection of the relevant bond distances, bond angles and torsion angles are listed in Table 1.

From the bond angles it can be seen that the oxaphosphete ring in **12** is highly strained and the trigonal bipyramidal geometry around the central phosphorus atom is considerably distorted due to the rigid spirocyclic system and due to the bulky P-substituent. It is noteworthy that the P–O bond is significantly elongated (1.989 Å versus the standard value of 1.585 Å[16]).

Two analogous heterocyclic derivatives have recently been described, spirocyclic 1,2-thiaphosphete **13**[17] and, as a transient bicyclic species, 1,2-azaphosphete **14**.[18]



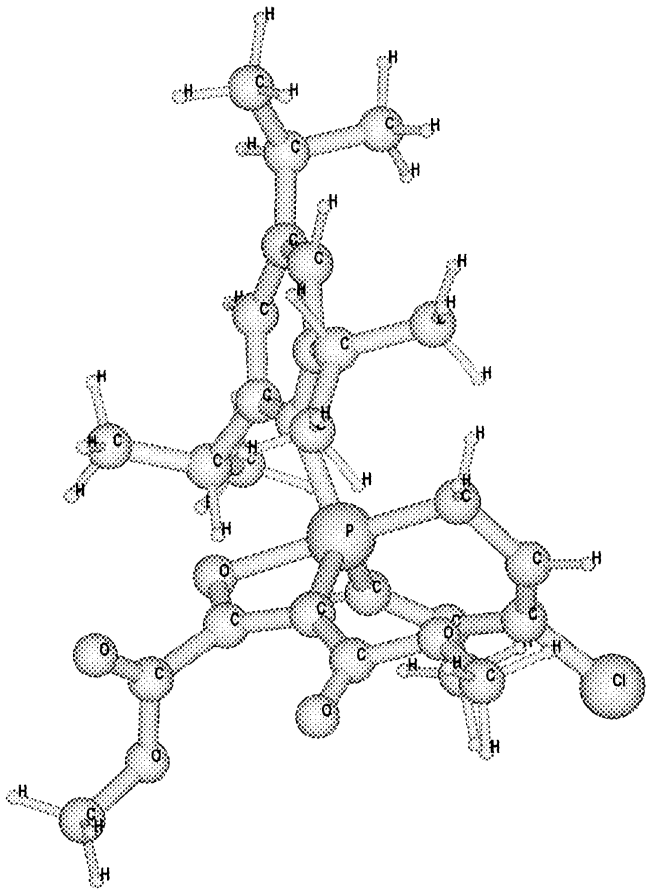
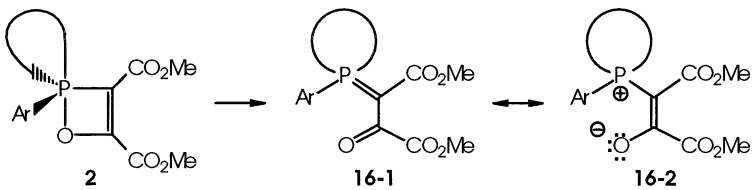



**Figure 1.**

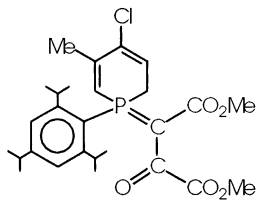
**Table 1.** Selected bond distances (Å), bond angles (°) and torsion angles (°) for oxaphosphete **12**

| Bond distance (Å) | | Bond angle (°) (difference from the ideal angle in degrees) | | Dihedral angle (°) | |
|---|---|---|---|---|---|
| $O_1$–$P_2$ | 1.989 | $P_2$–$O_1$–$C_4$ | 89.94 | $P_2$–$C_5$–$C_6$–Me | 178.25 |
| $P_2$–$C_3$ | 1.856 | $O_1$–$C_4$–$C_3$ | 108.13 | $P_2$–$C_5$–$C_6$–$C_7$ | −1.52 |
| $C_3$–$C_4$ | 1.378 | $C_4$–$C_3$–$P_2$ | 93.35 | $P_2$–$C_9$–$C_8$–$C_7$ | 30.53 |
| $C_4$–$O_1$ | 1.300 | $O_1$–$P_2$–$C_3$ | 68.58 (21.42) | $P_2$–$O_1$–$C_4$–$C_3$ | 0.55 |
| $P_2$–$C_5$ | 1.786 | $O_1$–$P_2$–$C_5$ | 90.48 (−0.48) | $P_2$–$C_3$–$C_4$–$O_1$ | −0.59 |
| $C_5$–$C_6$ | 1.340 | $O_1$–$P_2$–$C_{1'}$ | 87.38 (2.62) | | |
| $C_6$–$C_7$ | 1.460 | $C_5$–$P_2$–$C_9$ | 97.54 (−7.54) | | |
| $C_7$–$C_8$ | 1.344 | $C_3$–$P_2$–$C_9$ | 102.81 (−12.81) | | |
| $C_8$–$C_9$ | 1.468 | $C_{1'}$–$P_2$–$C_9$ | 94.60 (4.6) | | |
| $C_9$–$P_2$ | 1.877 | $O_1$–$P_2$–$C_9$ | 170.10 (9.90) | | |
| $P_2$–$C_{1'}$ | 1.889 | $C_5$–$P_2$–$C_{1'}$ | 113.95 (6.05) | | |
| | | $C_3$–$P_2$–$C_5$ | 112.21 (7.79) | | |
| | | $C_3$–$P_2$–$C_{1'}$ | 127.53 (−7.53) | | |




**Scheme 7.**

Attempted optimisation for the geometry of oxaphosphete **12** by AM1 semiempirical calculations[19] led to the opening of the strained four-membered ring to afford phosphorane **15**.




Further refinement of the above problem is in process. On the basis of the experimental data available, it cannot be phosphorane **15** that adequately represents the structure of the product derived from the [2+2] cycloaddition. On one hand, the spirocyclic structure (**12**) was confirmed by $^{13}C$ and $^{1}H$ NMR spectra, as well as by two-dimensional correlation diagrams.[2] The IR absorptions at $\nu = 756$ and 1678 $cm^{-1}$ also supported the oxaphosphete structure. On the other hand, the product in hand could not be titrated with hydroxylamine hydrochloride indicating that there is no keto carbonyl in the molecule. The product from the cycloaddition could not be utilised in the Wittig reaction either. If the product were a phosphorane (**15**), it should give the corresponding olefin ($PhCH{=}C(CO_2Me)C(O)CO_2Me$) on reaction with benzaldehyde. This was not, however, the case after a 2 day reflux with benzaldehyde in THF. It is a question to be examined if the oxaphosphete (**2**) can be converted to species **16** that may be represented by the phosphorane (**16-1**) and the stabilised ylide (**16-2**) resonance structures (Scheme 7). The ring opening would involve the break of a P–O bond with a bond energy of 407 kJ $mol^{-1}$. At the same time, the relief of ring strain may be a considerable driving force. The energy profile of the **2→16** transformation will also be studied.

It is worthy of mention that the only criterion of the novel [2+2] cycloaddition reaction that seems to be general for trialkylphenylphosphine oxides is the presence of the electron releasing aryl substituent on the phosphorus atom. The novel protocol gives a simple entry to valuable oxaphosphetes. Further work to clarify the theoretical background of the new cycloaddition and to study the reactivity of the oxaphosphetes is to be carried out soon.

## Acknowledgements

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4. Compound **3**: $\delta_P$ ($CDCl_3$) 64.2 (57%) and 63.6 (43%); HR-EI, $M^+_{found} = 320.2278$, $C_{20}H_{33}OP$ requires 320.2269.

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6. Compound **4**: $\delta_P$ ($CDCl_3$) 43.6; $\delta_C$ ($CDCl_3$) 20.7 ($J=18.1$, $C_6$-Me), 24.5 ($J=7.2$, $C_{6'}$-Me), 27.7 ($J=62.2$, $C_8$), 31.0 ($C(CH_3)_3$), 33.6 ($C(CH_3)_3$), 36.3 ($J=6.4$, $C_7$), 50.2 (MeO), 51.7 (MeO), 72.2 ($J=100.4$, $C_3$), 115.1 ($J=89.7$, $C_5$), 123.1 ($J=11.3$, $C^*_{3'}$), 124.3 ($J=87.4$, $C_{1'}$), 127.0 ($J=11.1$, $C^*_{5'}$), 142.3 ($J=10.0$, $C_{6'}$), 153.0 ($C_{4'}$), 153.4 ($J=7.4$, $C_{2'}$), 164.8 ($J=16.6$, $C_6$), 167.1 ($J=12.9$, C=O), 168.1 ($J=14.4$, C=O), 183.6 ($J=7.0$, $C_4$), * may be reversed; $\delta_H$ 5.98 (d, $J=28.0$, $C_5$-H); HR–FAB, $(M+H)^+_{found}=461.2445$, $C_{26}H_{38}O_5P$ requires 461.2457; IR (film) 1732, 1675, 757 $cm^{-1}$.
7. Compound **6**: $\delta_P$ ($CDCl_3$) 38.5 (58%) and 38.3 (42%); $\delta_C$ for $\mathbf{6_1}$ ($CDCl_3$) 19.6 ($J=16.8$, $C_6$-Me), 24.9 ($J=6.7$, $C_{6'}$-Me), 30.7 ($C(CH_3)_3$), 33.0 ($C(CH_3)_3$), 33.4 ($J=4.0$, $C_7$), 33.7 ($J=61.7$, $C_8$), 34.7 ($J=9.4$, $C_6$), 35.1 ($J=57.9$, $C_5$), 50.0 (MeO), 51.4 (MeO), 72.2 ($J=95.5$, $C_3$), 121.7 ($J=83.8$, $C_{1'}$), 124.5 ($J=12.0$, $C_{5'}$[a]), 126.1 ($J=10.0$, $C_{3'}$[a]), 142.8 ($J=8.3$, $C_{6'}$), 152.5 ($J=2.5$, $C_{4'}$), 154.4 ($J=7.5$, $C_{2'}$), 166.9 ($J=13.2$, C=O), 167.8 ($J=14.1$, C=O), 183.3 ($J=7.4$, $C_4$), $\delta_C$ for $\mathbf{6_2}$ ($CDCl_3$) 20.0 ($J=12.5$, $C_6$-Me), 24.8 ($J=6.8$, $C_{6'}$-Me), 29.2 ($J=57.2$, $C_8$), 30.7 ($C(CH_3)_3$), 33.0 ($C(CH_3)_3$), 33.6 ($J=6.6$, $C_7$), 34.1 ($J=7.7$, $C_6$), 39.7 ($J=58.3$, $C_5$), 50.0 (MeO), 51.4 (MeO), 71.8 ($J=95.8$, $C_3$), 122.1 ($J=83.9$, $C_{1'}$), 124.5 ($J=12.1$, $C_{5'}$[b]), 126.1 ($J=10.0$, $C_{3'}$[b]), 142.9 ($J=7.7$, $C_{6'}$), 152.5 ($J=3.1$, $C_{4'}$), 154.4 ($J=7.5$, $C_{2'}$), 167.0 ($J=13.2$, C=O), 167.8 ($J=14.1$, C=O), 183.2 ($J=7.3$, $C_4$), [a,b]may be reversed; $(M+H)^+_{found}=463.2588$, $C_{26}H_{40}O_5P$ requires 463.2613; IR (film) 1728, 1675, 757 $cm^{-1}$.
8. Compound **8**: $^{31}P$ NMR ($CDCl_3$) $\delta$ 26.4; $^{13}C$ NMR ($CDCl_3$) $\delta$ 16.7 ($J=17.8$ $C_6$-Me), 21.2 ($C_{4'}$-Me), 23.1 ($J=5.8$, $C_{2'}$-Me), 28.6 ($J=61.0$, $C_9$), 51.0 (MeO), 51.9 (MeO), 73.9 ($J=107.7$, $C_3$), 119.9 ($J=14.0$, $C_8$), 122.1 ($J=93.2$, $C_{1'}$), 122.8 ($J=84.8$, $C_5$), 131.1 ($J=12.1$, $C_{3'}$), 140.3 ($J=13.9$, $C_7$), 142.0 ($J=11.0$, $C_{2'}$), 142.7 ($C_{4'}$), 155.3 ($J=14.3$, $C_6$), 167.0 ($J=14.6$, C=O), 167.7 ($J=15.8$, C=O), 182.9 ($J=6.2$, $C_4$); HR–FAB, $(M+H)^+_{found}=423.1060$, $C_{21}H_{25}ClO_5P$ requires 423.1128 for the $^{35}Cl$ isotope; IR (film) 1732, 1660, 757 $cm^{-1}$.
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10. Compound **10a**: $\delta_P$ ($CDCl_3$) 28.6; HR–FAB, $(M+H)^+_{found}=451.2543$, $C_{25}H_{39}O_5P$ requires 451.2613; IR (film) 1731, 741 $cm^{-1}$.
11. Compound **10b**: $\delta_P$ ($CDCl_3$) 22.9; $\delta_C$ ($CDCl_3$) 15.7 ($J=15.8$, $CH_3$), 16.0 ($J=3.6$, $CH_2CH_3$), 23.6 ($CH(CH_3)_2$), 24.1 ($CH(CH_3)_2$), 24.8 ($CH(CH_3)_2$), 30.8 ($J=64.5$, $CH_2CH_2CH_3$), 31.8 ($CHMe_2$), 33.9 ($CHMe_2$), 51.9 (MeO), 52.5 (MeO), 73.1 ($J=86.1$, $C_3$), 122.9 ($J=11.3$, $C^*_{3'}$), 123.7 ($J=11.3$, $C^*_{5'}$), 165.6 ($J=13.1$, C=O), 165.9 ($J=13.4$, C=O), 183.0 ($C_4$), *may be reversed; $(M+H)^+_{found}=479.2800$, $C_{27}H_{44}O_5P$ requires 479.2926; IR (film) 1731, 745 $cm^{-1}$.
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