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First isolation and characterization of 1,2-oxaphosphetanes with three phenyl groups at the phosphorus atom in typical Wittig reaction using cyclopropylidenetriphenylphosphorane

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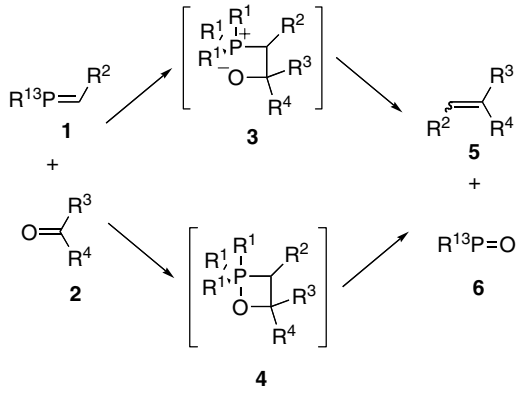
Abstract—1,2-Oxaphosphetanes bearing three phenyl groups directly bound to the phosphorus atom were successfully isolated for the first time as stable crystals in the typical Wittig reaction of cyclopropylidenetriphenylphosphorane with activated carbonyl compounds. X-ray analysis of the oxaphosphetane showed that the phosphorus atom is at the center of a slightly distorted trigonal bipyramidal structure. Thermal decomposition of these oxaphosphetanes was carried out to give the starting carbonyl compounds and Wittig reaction products, olefins.

The Wittig reaction is one of the most powerful methods for the preparation of carbon–carbon double bonds and is used as a key step in many natural product syntheses due to stereoselective formation of the double bond.[1] Because of its synthetic advantages, the stereoselectivity and mechanism of the Wittig reaction have long been studied. Earlier betaines **3** were believed to be the main intermediates in typical Wittig reactions (Scheme 1).

In 1973, however, Vedejs and co-workers succeeded in detection of only 1,2-oxaphosphetanes **4** at low temperature by NMR spectroscopy during typical Wittig reactions and observed that these intermediates decompose readily upon warming to room temperature into alkenes **5** and phosphine oxides **6**.[2] On the other hand, several stabilized, isolable oxaphosphetanes have been reported along with their X-ray structures.[3–10] Most of the previously reported stable oxaphosphetane structures contain fluorine-bearing or bicyclic phosphole-type ligands either at the phosphorus position or at the 4 position in the oxaphosphetane ring. Recently, Berger and coworkers studied Wittig reaction using 2-furylphenylphosphoranes **7** and found that 2-furyl groups on the phosphorus atom increase thermal stabilities of oxaphosphetanes and succeeded in isolation and determination of X-ray structure of tris(2-furyl) substituted oxaphosphetane, the stability of which is attributed to the electron-withdrawing properties of the 2-furyl group.[11,12]



Scheme 1.

Although triphenylphosphoranes are usually used as the most common reagents for typical Wittig reaction, only a few stable *P*,*P*,*P*-triphenyloxaphosphetanes have been isolated. However, a few isolated oxaphosphetanes reported are unusual oxaphosphetanes **8**[13] and **9**,[14]

Keywords: 1,2-Oxaphosphetanes; Wittig reaction; X-ray crystallographic analysis; Cyclopropylidenetriphenylphosphorane; Trigonal bipyramidal structure.
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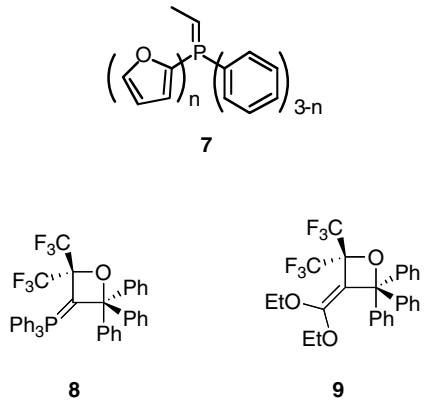


Scheme 2.

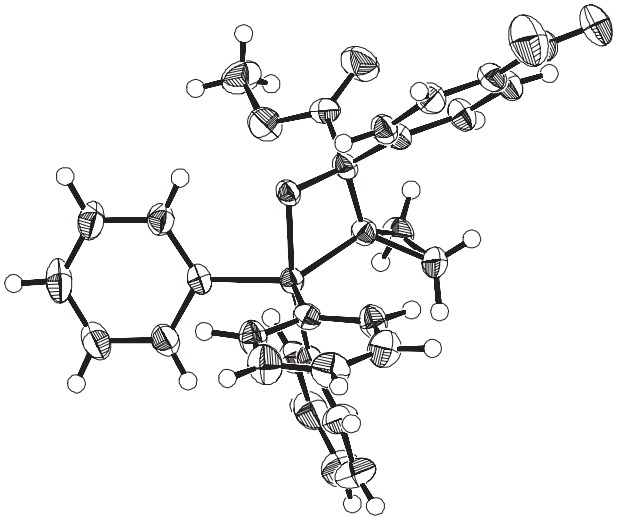


Figure 1. ORTEP drawing of **13a**.

which were not determined by X-ray analysis, as shown in Scheme 2.

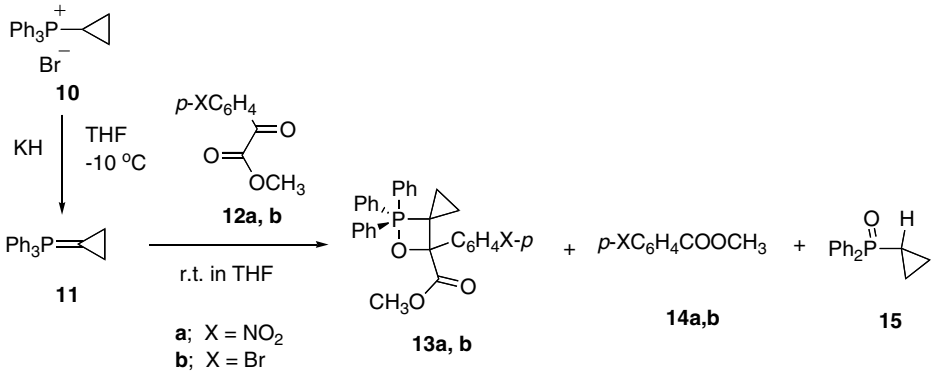
We would like to report that for the first time we succeeded in isolation and determination of X-ray structure of stable typical Wittig reaction intermediates *P*,*P*,*P*-triphenyloxaphosphetanes **13** in the reaction of cyclopropylidenetriphenylphosphorane **11** with dicarbonyl compounds **12**.

To a suspension of triphenylcyclopropylphosphonium bromide **10** (3.84 g, 10 mmol) in THF at −12 °C was added 30% potassium hydride (2.02 g, 15 mmol) and stirred for 30 min, then stirred for 20 h at room temperature. To the resultant yellow solution was added 2.09 g of methyl *p*-nitrobenzoylformate **12a** and stirred at room temperature for 2 h. The reaction mixture was poured into methanol. The reaction mixture was chromatographed over silica gel using benzene and ethyl acetate as eluents to give an 1,2-oxaphosphetane **13a** in 38 % yield along with methyl *p*-nitrobenzoate **14a** (5%) and cyclopropyldiphenylphosphine oxide **14** (38%) (Scheme 3).

The structure of the oxaphosphetane **13a** was determined by X-ray analysis as shown in Figure 1.[15] The phosphorus atom is at the center of a slightly distorted trigonal bipyramidal structure, the angle between the two apical positions and the phosphorus atom being 166.6°. The four-membered oxaphosphetane ring is in an apical equatorial position and is almost coplanar, as its dihedral angle is 1.0°. ^{31}P NMR spectrum of **13a** was observed around at −46.2 ppm, which is ^{31}P chemical shift regions typical for pentavalent phosphorus species. ^{13}C NMR spectrum of **13a** in $CDCl_3$ showed equivalency of three phenyl groups, indicating fast rotation of the groups attached to the phosphorus atom in solution.[16] At the present time, it is vague how methyl *p*-nitrobenzoate **14a** was formed.

The reaction of **11** with methyl bromobenzoylformate **12b** gave the oxaphosphetane **13b** (15%), methyl *p*-bromobenzoate **14b** (8%), and cyclopropyldiphenylphosphine oxide **15** (20%).

During recrystallization of **13a** at room temperature over a month, **13a** decomposed to yellow phosphonium salt **16a**, almost quantitatively. The structure of the salt **16a** was determined by X-ray analysis. The formation of the salt **16a** suggests that the oxaphosphetane slowly dissociated at room temperature into the starting materials, the phosphorane **11** and the ketoester **12a**. The X-ray structure of the starting cyclopropylidenephosphorane **11** reported that the angle between the bond P–C and cyclopropyl ring is very close to that of the oxaphosphetane **13a** (Scheme 5).[17]



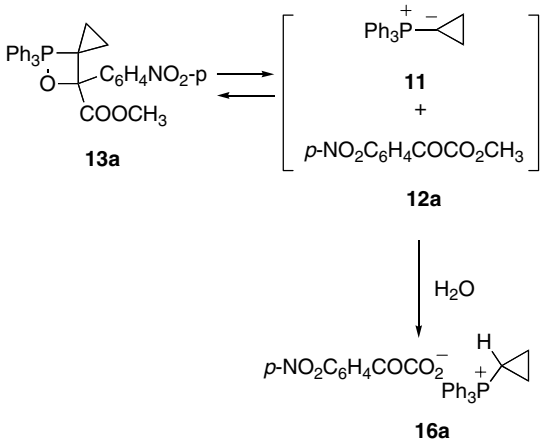
Scheme 3.

The reaction of **11** with methyl benzoylformate, methyl *p*-toluoylformate, methyl *p*-anisoylformate was carried out, but in most cases, the starting materials were recovered.

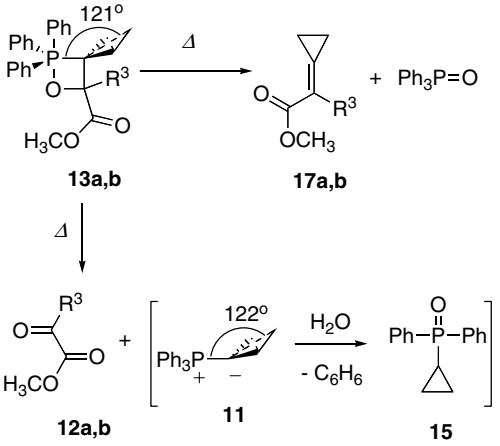
The reaction of **11** with *p*,*p*′-dichlorobenzil **12c** also gave the corresponding oxaphosphetane **13c**. However, oxaphosphetanes were not obtained from benzil and α-furil.

The reason for isolation of *P*,*P*,*P*-triphenyloxaphosphetanes **13** seem to be attributed to high transition state activation energy for process to olefins due to the product being highly strained methylenecyclopropane **17**.

Quantitative dissociation of **13a** to the starting materials **11** and **12a** on standing at room temperature prompts us to study the thermolysis of the *P*,*P*,*P*-triphenyloxaphosphetanes **13a**,**b**. Thermolysis of the oxaphosphetane **13a**,**b** was carried out at several temperatures to give the starting oxophenylacetates **12a**,**b**, cyclopropyldiphenylphosphine oxide **15**, Wittig reaction products, cyclopropylidenephenylacetate derivatives **17a**,**b**, and triphenylphosphine oxide as shown in Scheme 4 (Table 1).



Scheme 4.



Scheme 5.

Table 1. Ratios of methyl phenyloxoacetates **12a**,**b** and olefins **17a**,**b** on the thermolysis of oxaphosphetanes **13a**,**b** at several temperatures

Temperature (°C)	**12**/**17** ratio[a] (total yield/%)[a]	
	13a	**13b**
80	68/32 (73)	53/47 (89)
90	60/40 (77)	49/51 (97)
100	37/63 (61)	45/55 (93)

[a] Determined by ^{1}H NMR.

In conclusion, we have shown that, for the first time, we succeeded in isolation of stable 1,2-oxaphosphetanes **13** bearing three phenyl groups directly bound to the phosphorus atom using cyclopropylidenetriphenyl–phosphorane **11** in Wittig reaction with some dicarbonyl compounds **12a**–**c**, and in determination of X-ray structure of **13a**.

References and notes

1. (a) Nicolaou, K. C.; Härter, M. W.; Gunzer, J. L.; Nadin, A. *Liebigs Ann./Recueil* **1997**, 1283; (b) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.
2. (a) Vedejs, E.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778; (b) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823; (c) Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Almond, H. R., Jr.; Whittle, R. R.; Olofson, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 7664.
3. Ul-Haque, M.; Caughlan, C. N.; Ramirez, F.; Pilot, J. F.; Smith, C. P. *J. Am. Chem. Soc.* **1971**, *93*, 5229.
4. Kawashima, T.; Kato, K.; Okazaki, R. *J. Am. Chem. Soc.* **1992**, *114*, 4008.
5. (a) Kawashima, T.; Kato, K.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *105*, 941; (b) Kawashima, T.; Kato, K.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 869.
6. Kawashima, T.; Takami, H.; Okazaki, R. *J. Am. Chem. Soc.* **1994**, *116*, 4509.
7. Kawashima, T.; Okazaki, R.; Okazaki, R. *Angew. Chem., Int. Ed.* **1997**, *36*, 2500.
8. Bestmann, H. J.; Roth, K.; Wilhelm, E.; Böme, R.; Burzlaff, H. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 876.
9. Aly, H. A. E.; Barlow, J. H.; Russell, D. R.; Smith, D. J. H.; Swindles, M.; Trippett, S. *J. Chem. Soc., Chem. Commun.* **1976**, 449.
10. Kojima, S.; Sugino, M.; Matsukawa, S.; Nakamoto, M.; Akiba, K. *J. Am. Chem. Soc.* **2002**, *124*, 7674.
11. Appel, M.; Blaurock, S.; Berger, S. *Eur. J. Org. Chem.* **2002**, 1143.
12. Andersen, N. G.; Keay, B. A. *Chem. Rev.* **2001**, *101*, 997.
13. Birum, G. H.; Matthews, C. N. *J. Chem. Soc., Chem. Commun.* **1967**, 137.
14. Saalflank, R. W.; Paul, W.; Liebenow, H. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 713.
15. Crystallographic data for the compound **13a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 281955. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
16. Compound **13a**: ^{13}C NMR(BCM) in $CDCl_3$: 174.2 (d, $J = 5.0$ Hz), 148.8 (d, $J = 6.7$ Hz), 147.1 (s), 137.8 (d, $J = 96.7$ Hz), 132.7 (d, $J = 8.9$ Hz), 129.1 (s), 127.4 (d, $J = 12.3$ Hz), 127.2 (s), 122.7 (s), 73.7 (d, $J = 3.5$ Hz), 52.3

(s), 49.0 (d, $J = 123.5$ Hz), 8.5 (d, $J = 3.4$ Hz); ^{31}P NMR: δ −46.2.

Compound **13b**: ^{13}C NMR(BCM) in $CDCl_3$: 174.8 (d, $J = 4.5$ Hz), 140.3 (d, $J = 7.3$ Hz), 148.2 (d, $J = 96.1$ Hz), 132.8 (d, $J = 8.9$ Hz), 130.8 (s), 128.9 (d, $J = 2.2$ Hz), 127.9 (s), 127.3 (d, $J = 12.3$ Hz), 121.3 (s), 73.7 (d, $J = 3.5$ Hz), 52.3 (s), 48.6 (d, $J = 122.4$ Hz), 8.6 (s); ^{31}P NMR: δ −46.2.

Compound **13c**: ^{13}C NMR(BCM) in $CDCl_3$: 201.4 (d, $J = 1.7$ Hz), 140.6 (d, $J = 9.5$ Hz), 138.3 (d, $J = 96.1$ Hz), 137.9 (s), 134.1 (s), 133.0 (s), 132.8 (d, $J = 8.9$ Hz), 131.2 (s), 128.9 (d, $J = 2.2$ Hz), 128.5 (s), 127.6 (s), 127.3 (d, $J = 11.7$ Hz), 127.0 (s), 77.2 (s), 48.7 (d, $J = 121.3$ Hz), 7.9 (d, $J = 5.6$ Hz); ^{31}P NMR: δ −46.9.

17. Schmidbaur, H. S.; Schier, A.; Milewski-Mahrla, B.; Schubert, U. *Chem. Ber.* **1982**, *115*, 722.