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Revised Structure of 2-Cyclohexyl-3,4-diphenyl-1,2-oxaphosphetane 2-Oxide

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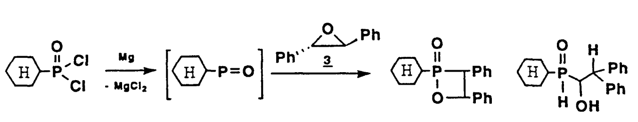
Synopsis. The correct structure of the title compound was elucidated to be cyclohexyl(2,2-diphenyl-1-hydroxyethyl)phosphine oxide, which seems to be formed via migration of a phenyl group, from the NMR spectral data and synthesis of the dimethyl derivative.

In the course of our study on the reactions of phosphinylidenes and phosphinothioylidenes,1) we have reported that 1,2-oxaphosphetane derivative (**1**) was formed in the reaction of cyclohexylphosphonic dichloride (**2**) with magnesium in the presence of *trans*-stilbene oxide (**3**) as shown in the following scheme.2)



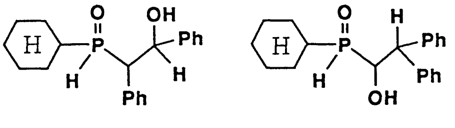
2 **1** **4**

Further investigation on this compound allows us to reach the conclusion that the product is not 1,2-oxaphosphetane 2-oxide (**1**), but an acyclic secondary phosphine oxide (**4**), which seems to be formed via migration of a phenyl group. In this paper we wish to revise the structure.

Results and Discussion

In order to confirm whether the sample, which was obtained previously,2) remains unchanged as it was or not, we took a ^{1}H NMR spectrum (90 MHz). Its spectrum showed the same signals as taken previously except a double doublet with a large coupling constant, indicating the existence of a direct P-H bond. We overlooked a double doublet in the 60 MHz-^{1}H NMR spectrum, because a lower field signal had appeared about δ=9.7 and upper one, which was expected to appear at δ=2.2, was unfortunately superimposed with the signals of the cyclohexyl group. In the IR spectrum the stretching frequencies for O-H and P-H bonds had been observed at 3150 and 2330 cm^{-1}, respectively. However, the former band had been assigned to that of water of crystallization, as expected from the results of elemental analysis, and the latter band had been completely neglected because the presence of P-H bond was beyond the consideration. Judging from the existence of P-H bond we at first presumed Structure A, which is considered to be formed by the reduction and the subsequent ring opening by hydrolysis of the oxaphosphetane.

The ^{13}C NMR spectrum showed the signals due to three methine groups at δ_C=34.54 (J=65.4 Hz), 53.31 (J=3.4 Hz), and 69.74 (J=74.5 Hz). The chemical shifts are reasonable for the carbons bonding to a phosphorus, phosphorus, and oxygen atom, respectively, but the magnitudes of coupling constant with phosphorus nucleus cannot be explained for Structure A at all. From the data a phosphorus atom must directly be attached to the carbon bonded with an oxygen atom. Structure B (**4**) is consistent with these facts (see Fig. 1).



Structure A Struucture B (**4**)

Fig. 1. Possible Structures of the Product.

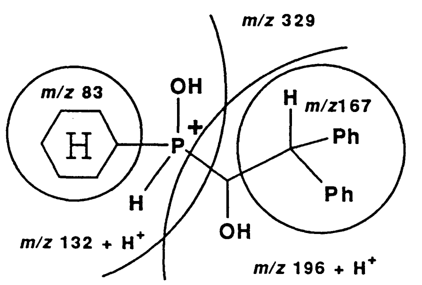
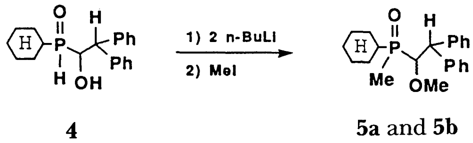


Fig. 2. Fragmentation of **4**.

The ^{31}P NMR spectrum showed a very small peak at δ_P=44.96 (<1/18) due to a minor diastereomer besides a major peak at δ_P=39.11. A negligibly small doublet was observed at δ=6.14 in the ^{1}H NMR spectrum, suggesting the formation of diastereomer also. Interesting features in the NMR spectrum are nonequivalences in cyclohexane ring carbons and in two phenyl groups, because of neighboring chiral center.

On the other hand the mass spectrum measured by electron impact ionization gave no parent peak, as mentioned previously,2) but in the chemical ionization mass spectrum using methane gas the protonated molecular peak was observed at m/z 329 (7%). The base peak was m/z 105, which is assigned to a rearranged fragment (PhCO$^+$). Peaks at m/z 197 (14%), 167 (44%), 133 (46%), and 83 (51%) were also observed, supporting the structure **4** (see Fig. 2).

Methylation of 4. Compound **4** was allowed to react with 2 equivalents of *n*-BuLi at −78 °C in tetrahydrofuran (THF) and with excess iodomethane to afford a mixture of cyclohexyl(methyl)(2,2-diphenyl-1-methoxyethyl)phosphine oxides (**5a** and **5b** in 3 : 1



4 **5a** and **5b**

diastereomer ratio. The structure of **5** was determined by the observations of a pair of doublets at δ=0.84 and 0.98 due to PMe groups and a pair of singlets at δ=3.22 and 3.30 due to OMe groups instead of the signals due to PH and OH groups in the ^{1}H NMR spectrum. In the ^{13}C NMR spectrum of **5** the signals of the minor diastereomer could not be observed clearly, because of an insufficient amount of the sample, but those of the major one support the structure **5**. The high resolution mass spectrum gave the exact mass number of the parent peak. The change in the diastereomer ratio can be explained reasonably if one considers the difference in sterical bulkiness between hydrogen atom and methyl group.

It is very surprising that such a secondary alkylphosphine oxide remains without any change even after being exposed to air for 14 years. Unexpected stability of this compound having a readily oxidizable moiety seems to come from the following factors: intramolecular hydrogen bonding stabilizes a pentavalent tautomer and a reaction center is hindered by two bulky substituents.

Experimental

^{1}H NMR spectra were measured with a Bruker AM-500 (500.13 MHz) spectrometer using tetramethylsilane (TMS) as an internal standard. ^{13}C NMR spectra were taken with a Bruker AM-500 (125.77 MHz) spectrometer using TMS as an internal standard. ^{31}P NMR spectra were obtained with a JEOL FX-90Q spectrometer using 85% H_3PO_4 as an external standard. IR spectra were taken with a Hitachi 260-30 spectrophotometer. Mass spectra were recorded with a JEOL 300-D mass spectrometer.

The sample stored in a vial, which was reported to be 2-cyclohexyl-3,4-diphenyl-1,2-oxaphosphetane 2-oxide (**1**),[2] was used after confirming it remains unchanged as it was.

Spectral Data of the Compound 4. ^{1}H NMR ($CDCl_3$)[3] (500.13 MHz) δ=1.10—1.14 (4H, m, C(2)$\underline{H}_2$, ax. H-C(3′), and eq. H-C(4) of c-Hex), 1.65—1.70 (2H, m, C(3)$\underline{H}_2$ of c-Hex), 1.70—1.80 (3H, m, C(2′)$\underline{H}_2$ and eq. H-C(4) of c-Hex), 1.80—1.95 (1H, m, C(1)$\underline{H}$ of c-Hex), 1.95—2.05 (1H, m, eq. H-C(3′) of c-Hex), 4.25 (1H, s, O$\underline{H}$), 4.50—4.60 (2H, m, C$\underline{H}$C$\underline{H}$OH), 6.02 (1H, dd, $^3J_{H,H}$=4.8 Hz, $^1J_{H,P}$=451.1 Hz, P$\underline{H}$), 7.20—7.25 (2H, m, para-H of Ph and Ph′), 7.28—7.31 (2H, m, meta-H of Ph), 7.32—7.36 (4H, m, meta and ortho-H of Ph′), and 7.43—7.45 (2H, m, ortho-H of Ph). A small doublet appeared at δ=6.14 ($^1J_{H,P}$=458.6 Hz). ^{13}C NMR ($CDCl_3$)[3] δ_C=25.16 (s,[4] C-4 of c-Hex), 25.22 (d, $^3J_{C,P}$=2.9 Hz, C-3′of c-Hex), 25.73 (s, C-2 of c-Hex), 25.80 (d, $^3J_{C,P}$=14.8 Hz, C-3 of c-Hex), 25.91 (d, $^2J_{C,P}$=12.8 Hz, C-2′ of c-Hex), 34.54 (d, $^1J_{C,P}$=65.4 Hz, C-1 of c-Hex), 53.31 (d, $^2J_{C,P}$=3.4 Hz, PCHC$\underline{H}$Ph$_2$), 69.74 (d, $^1J_{C,P}$=74.5 Hz, P$\underline{C}$HOH), 126.92 (s, para-C of Ph), 127.48 (s, para-C of Ph′), 128.49 (s, ortho-C of Ph′), 128.69 (s, ortho-C and meta-C of Ph), 129.06 (meta-C of Ph′), 139.91 (s), and 140.35 (d, $^3J_{C,P}$=10.5 Hz) (ipso-C of Ph and Ph′). ^{31}P NMR ($CDCl_3$) δ_P=39.11 and 44.96 (>18 : 1). Mass spectrum (chemical ionization : Methane gas): *m/z* 329 (M^++1, 7%), 197 ($HCOCHPh_2+H^+$, 14), 167 (CH^+Ph_2, 44), 133 (c-$C_6H_{11}P(O)H_2+H^+$, 46), 105 ($PhCO^+$, 100), and 83 (c-$C_6H_{11}^+$, 51). IR (KBr disc) ν_{OH}=3150 cm^{-1} and ν_{PH}=2330 cm^{-1}.

Methylation of 4. To a solution of **4** (7.2 mg, 0.022 mmol) in THF (2 ml) was added dropwise *n*-BuLi (0.96 M hexane solution, 0.05 ml, 0.048 mmol) at −78 °C with stirring, then excess of iodomethane (0.1 ml, 1.6 mmol) was added to the solution. The reaction mixture was allowed to warm to room temperature, treated with aq NH_4Cl. Organic layer was extracted with dichloromethane and dried over anhydrous $MgSO_4$. After removal of the solvent the residue was subjected to high-pressure liquid chromatography (column: Japan Analytical Industries (JAIGEL 1H, 2H)) to give a diastereomer mixture of cyclohexyl(methyl)(2,2-diphenyl-1-methoxyethyl)phosphine oxides (**5a** and **5b**) (2.0 mg, 26%) as viscous oil in a ratio of 3 : 1. **5:** ^{1}H NMR ($CDCl_3$) δ=0.84 (d, $^2J_{H,P}$=12.4 Hz, PC$\underline{H}_3$ of **5b**), 0.98 (d, $^2J_{H,P}$=11.9 Hz, PC$\underline{H}_3$ of **5a**), 0.80—1.35 (m) and 1.55—1.92 (m) (c-$C_6\underline{H}_{11}$ of **5a** and **5b**), 3.22 (s, OC$\underline{H}_3$ of **5b**), 3.30 (s, OC$\underline{H}_3$ of **5a**), 4.26 (dd, $^3J_{H,H}$=7.1 Hz, $^2J_{H,P}$=4.9 Hz, PC$\underline{H}$OMe of **5a**), 4.29 (t, $^3J_{H,H}$=$^3J_{H,P}$=5.1 Hz, PC$\underline{H}$OMe of **5b**), 4.56 (t, $^3J_{H,H}$=$^3J_{H,P}$=7.1 Hz, C$\underline{H}$Ph$_2$ of **5a**), 4.66 (t, $^3J_{H,H}$=$^3J_{H,P}$=5.1 Hz, C$\underline{H}$Ph$_2$ of **5b**), 7.20—7.24 (m, all para-H), 7.24—7.35 (m, all meta-H), 7.42—7.46 (m, ortho-H of Ph of **5a** and **5b**), 7.52—7.55 (m, ortho-H of Ph′ of **5a**), and 7.57—7.62 (m, ortho-H of Ph′ of **5b**). ^{13}C NMR ($CDCl_3$) δ_C=10.13 (d, $^1J_{C,P}$=59.9 Hz, P$\underline{C}$H$_3$), 24.76 (d $^4J_{C,P}$=3.6 Hz, C-4 of c-Hex), 25.98 (d, $^3J_{C,P}$=2.5 Hz, C-3′ of c-Hex), 26.23 (d, $^3J_{C,P}$=8.4 Hz, C-3 of c-Hex) , 26.31 (s, C-2 of c-Hex), 26.35 (d, $^2J_{C,P}$=4.9 Hz, C-2′ of c-Hex), 36.71 (d, $^1J_{C,P}$=64.0 Hz, C-1 of c-Hex), 51.11 (d, $^2J_{C,P}$=5.8 Hz, $\underline{C}$HPh$_2$), 60.68 (s, O$\underline{C}$H$_3$), 83.36 (d, $^1J_{C,P}$ =76.3 Hz, P$\underline{C}$HOMe), 127.00 (s, para-C of Ph), 127.07 (s, para-C of Ph′), 128.44 (s, ortho-C of Ph), 128.73 (s, meta and ortho-C of Ph′), 129.53 (s, meta-C of Ph), 140.29 (s), and 141.3 (d, $^3J_{C,P}$=5.7 Hz) (ipso-C of Ph and Ph′). ^{31}P NMR ($CDCl_3$) δ_P=51.28 and 51.64 (ca. 3 : 1). High resolution mass spectrum (70 eV): *m/z* Found: 356.1895. Calcd for $C_{22}H_{29}O_2P$: 356.1905.

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References

1) For examples see: M. Yoshifuji, S. Nakayama, R. Okazaki, and N. Inamoto, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 2065, 2067 and references cited therein.

2) S. Nakayama, M. Yoshifuji, R. Okazaki, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **49**, 1173 (1976).

3) These assignments are supported by ^{1}H-{^{31}P} and ^{13}C-{^{31}P} NMR and two-dimensional NMR (H,H-COSY and C,H-COSY (correlation spectroscopy)) spectroscopies.

4) Abbreviation shows a coupling manner with a phosphorus nucleus.