# Synthesis and Novel Mass Spectral Rearrangements of 10-Phenylphenoxaphosphine and Some of its Derivatives

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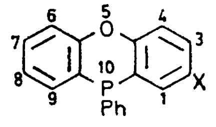
The successive treatment of phenyl ether with n-butyl-lithium and phenylphosphonous dichloride afforded virtually, in a one-step process, the title compound. The mass spectrum of the cyclic phosphine (Ia) was characterized by the loss of phenyl followed by a one-step elimination of both heteroatoms. Anchimeric assistance of the oxygen in the phenyl expulsion was supported by energetic considerations and by the observed one-step elimination of $C_6H_5O\cdot$ from the molecular ion of (Ia). A similar rearrangement was exhibited by bis-(*o*-methoxyphenyl)-phenylphosphine (IV), leading also to a rearranged carbon skeleton. The phosphine oxide (IIa) and sulphide (IIIa) exhibited rearrangements leading to the expulsion of $C_6H_5O\cdot$ and $C_6H_5S\cdot$ from the corresponding molecular ions.

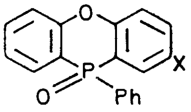
THE phenoxaphosphine system (I) has attracted both theoretical[1] and biological[2] interest, it being the phosphorus analogue of the phenoxazine skeleton. The first synthesis of a derivative of this system[1] was that of the title compound. The key intermediate was 2,2′-dibromodiphenyl ether, which was converted into the dilithio-derivative; this, in turn, was treated with phenylphosphonous dichloride to yield the desired heterocyclic phosphine. Alternative methods were developed which were based on either activation of an *ortho*-position of the aromatic ether by a diazonium group[3] or protection of both *para*-positions,[4] and then reaction with various phosphorus halides and a catalyst.

Since aromatic ethers were shown to be lithiated by n-butyl-lithium at the *ortho*-position,[5] it seemed attractive to use this advantage in simplifying the synthesis of phenoxaphosphine derivatives.[6,7] Indeed, phenyl ether, when treated with n-butyl-lithium followed by phenylphosphonous dichloride, yielded the phosphine (Ia), thus providing essentially a one-step synthesis of (Ia) from phenyl ether. The 2,2′-dilithiodiphenyl ether, being apparently an intermediate, was prepared in THF–ethyl ether as the solvent,[8] thus enabling reduction of the reaction time from 72 h (when prepared in ethyl ether[5]) to 5 h.

The utility of the *ortho*-lithiation for the synthesis of otherwise not easily accessible aromatic phosphines was further exemplified by obtaining bis-(*o*-methoxyphenyl)-phenylphosphine (IV) from the reaction of anisole with n-butyl-lithium followed by phenylphosphonous dichloride. Derivatives such as (II) and (III) were prepared by conventional methods. (See Experimental section.)

(I)

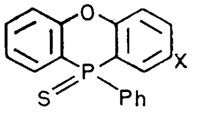


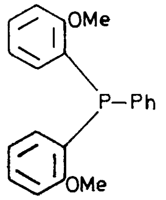


(II)

a; X = H , b; X = Cl

(III)





(IV)

It appeared of interest to study the mass spectra of the unsubstituted phenoxaphosphine derivatives, as well as those of the 2-chloro-analogues (Ib)—(IIIb),[3] since only 2,8-disubstituted derivatives have been examined so far.[9] On the strength of metastable

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* Address as of 1.1.1972; Israel Institute for Biological Research, Ness-Ziona, Israel.

[1] F. G. Mann and I. T. Millar, *J. Chem. Soc.*, 1953, 3746.

[2] I. Granoth, A. Kalir, and Z. Pelah, *Israel J. Chem.*, 1968, **6**, 651.

[3] J. B. Levy, L. D. Freedman, and G. O. Doak, *J. Org. Chem.*, 1968, **33**, 474.

[4] I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Tetrahedron*, 1970, **26**, 813, and references cited therein.

[5] K. Oita and H. Gilman, *J. Amer. Chem. Soc.*, 1957, **79**, 339.

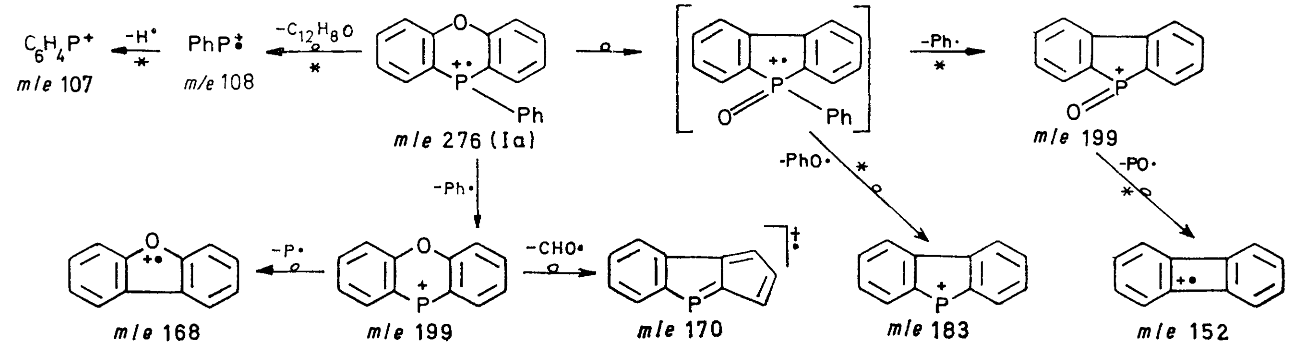
[6] F. G. Mann, ‘The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, and Bismuth,’ Wiley–Interscience, 2nd edn., 1970, p. 289.

[7] J. B. Levy, W. C. Laughlin, J. C. Bird, and F. G. Mann, *J. Elisha Mitchell Sci. Soc.*, 1969, **85**, 120.

[8] H. Gilman and W. J. Trepka, *J. Org. Chem.*, 1961, **26**, 5202.

[9] I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Israel J. Chem.*, 1970, **8**, 621.

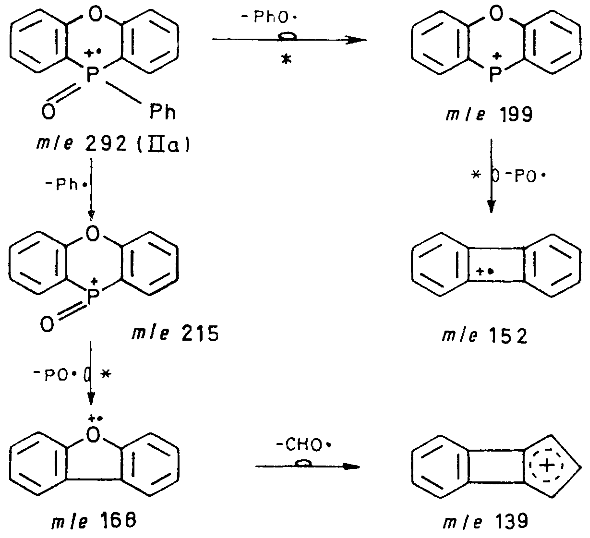
transition characteristics and exact mass measurements, the fragmentation paths shown in Schemes 1 and 2 were established. It appeared that the loss of $C_6H_5\cdot$ from the molecular ion of (Ia) occurred mainly with an anchimeric assistance of the oxygen or even preceded by the migration of the oxygen to the phosphorus. The above reaction was the lowest energy process, for which a very intense metastable transition was observed: $[m^*]/[d]\% = 0{\cdot}11$. This observation indicated a relatively slow reaction, probably a rearrangement.[10,11] Furthermore, the elimination of $C_6H_5O\cdot$ from the molecular ion of (Ia) to produce *m/e* 183 (Scheme 1) suggested again extensive rearrangement prior to decomposition. The participation of the ether functional group in the $C_6H_5\cdot$ elimination seemed to be the first reported example of anchimeric assistance in the mass spectral fragmentations of phosphorus compounds. Nevertheless, there must have been another fragmentation mode, apparently with a higher activation energy, in which a direct cleavage of the P–$C_6H_5$ bond took place, followed by the loss of P· to give *m/e* 168 (Scheme 1), since the latter reaction was accompanied by a suitable metastable transition.



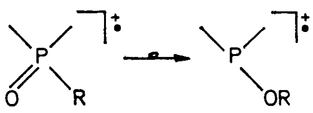
SCHEME 1

Similar fragmentation patterns were observed for (Ib). The ion *m/e* 170 was common in the spectra of both phosphines (Ia) and (Ib). Expulsion of CHO· from *m/e* 199 in the case of (Ia) and loss of ClCO·[12] from *m/e* 233 for (Ib) could account for that.

The phosphine oxides (IIa) (Scheme 2) and (IIb) lost $C_6H_5\cdot$ in a reaction with a relatively high activation energy, and no metastable transitions were observed for this process in either case. The electron-impact induced phosphine oxide–phosphinite rearrangement (1) was established by appropriate metastable transitions for the loss of $C_6H_5O\cdot$ from the molecular ions of (IIa) and (IIb) and by exact mass measurements of the daughters. This reaction had been observed in the analogous phenothiaphosphine oxides,[13] and it seems to be fairly general for R = aryl and H (ref. 9) but not for R = $CH_3$.[9] The $M - 1\ \rceil^+$ ions are very prominent in the spectra of (IIa) and (IIb) but are only of moderate intensity in the spectra of (Ia) and (Ib). No further fragmentation of the $M - 1\ \rceil^+$ ions could be found. This loss of a hydrogen proceeded with the lowest activation energy and appeared to be a rearrangement: $[m^*]/[d]\% = 1{\cdot}0$.[10] Abundant $M - 1\ \rceil^+$ ions have been reported for aromatic phosphinic acids[14] and for triphenylphosphine oxide[15] and were shown to involve cyclization of (V) to (VI), for example:



SCHEME 2



(1)

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[10] F. W. McLafferty and R. B. Fairweather, *J. Amer. Chem. Soc.*, 1968, **90**, 5915.

[11] I. Howe in 'Mass Spectrometry: Specialist Periodical Reports,' ed. D. H. Williams, The Chemical Society, London, 1971, vol. 1, p. 38.

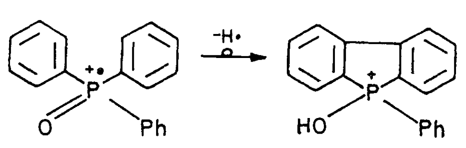
[12] I. Granoth and J. B. Levy, *J. Chem. Soc.* (*B*), 1971, 2391.

[13] I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Org. Mass Spectrum*, 1970, **3**, 1359.

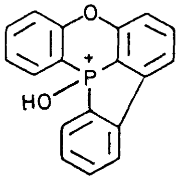
[14] P. Haak, M. J. Frearson, and C. E. Diebert, *J. Org. Chem.*, 1969, **34**, 788.

[15] D. H. Williams, R. S. Ward, and R. G. Cooks, *J. Amer. Chem. Soc.*, 1968, **90**, 966.

(V)



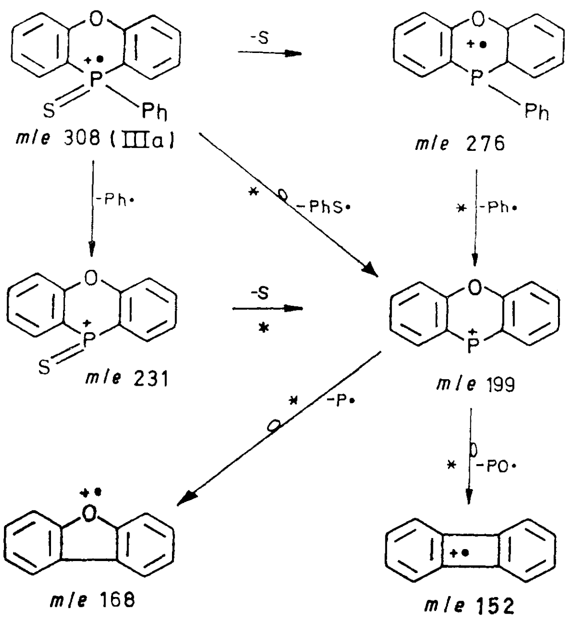
(VI)



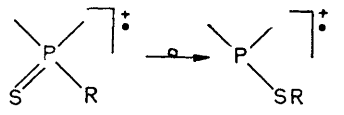
(VII)

A structure such as (VII) could account for the stability of $M - 1 \rceil^{+}$ and for the high steric requirements, which were reflected in the reaction taking place to a large extent in the second field-free region.

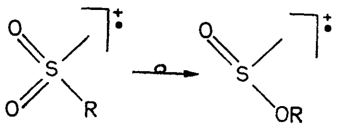
The mass spectra of the sulphides (IIIa) and (IIIb) showed only two intense peaks, $M^{+\cdot}$ and $M - C_6H_5S \rceil^{+}$, the latter being the base peak. The fragmentation paths are illustrated in Scheme 3. The loss of $C_6H_5S\cdot$ from the molecular ions of (IIIa) and (IIIb) was apparently preceded by a novel rearrangement of a phosphine sulphide-thiophosphinite type (2). This rearrangement occurred also in the molecular ion of triphenylphosphine sulphide.† Reactions of similar nature are the loss of $C_6H_5O\cdot$ from the phosphine oxides [as found for (IIa) and (IIb)] and the migration of a group from sulphur to oxygen in sulphoxides and sulphones [reaction (3)].[16]



SCHEME 3



(2)



(3)

It had been demonstrated[15] that the cyclization of triphenylphosphine under electron impact to produce the $M - 1 \rceil^{+}$ ion involved the specific loss of an *ortho*-hydrogen. In the case of bis-(*o*-methoxyphenyl)phenylphosphine (IV), the intensity of $M - 1 \rceil^{+}$ is 12% and of $M - CH_3O \rceil^{+}$ is 30% of the base peak ($M^{+}$). This remarkable elimination of $CH_3O\cdot$ from the molecular ion of (IV) is even more pronounced in the generally similar mass spectrum of bis-(*o*-methoxyphenyl)phenylphosphine oxide, where $M - CH_3O \rceil^{+}$ is 78% and $M - 1 \rceil^{+}$ is only 21% of the intensity of the base peak ($M^{+\cdot}$). This *ortho*-effect is impressive, since the loss of $CH_3O\cdot$ from the molecular ion of anisole is of minor importance.[17] Furthermore, the phosphine (IV) and its oxide lost neither $CH_3\cdot$ nor $CH_2O$, which were typical fragmentations of anisole.[17] On the other hand, it appeared from the low-resolution spectrum of (IV) that not only cyclization, leading eventually to the formation of *m/e* 183, but at least another rearrangement might have been involved. Indeed, exact mass measurements established the composition of the abundant ions in the mass spectrum of (IV) as shown in the Table.

Relative intensity and composition of the principal peaks in the mass spectrum of bis-(*o*-methoxyphenyl)phenylphosphine (IV)

| *m/e* Calculated | Measured | Composition | Relative intensity |
|---|---|---|---|
| 322·1122 | 322·1132 | $C_{20}H_{19}O_2P$ | 100 |
| 321·1044 | 321·1047 | $C_{20}H_{18}O_2P$ | 12 |
| 291·0938 | 291·0935 | $C_{19}H_{16}OP$ | 30 |
| 231·0574 | 231·0566 | $C_{13}H_{12}O_2P$ | 16 |
| 213·0468 | 213·0468 | $C_{13}H_{10}OP$ | 13 |
| 199·0312 | 199·0299 | $C_{12}H_8OP$ | 24 |
| 183·0363 | 183·0363 | $C_{12}H_8P$ | 43 |
| 152·0 | — | $C_{12}H_8$ | 13 |
| 137·0155 | 137·0147 | $C_7H_6OP$ | 10 |
| 121·0653 | 121·0645 | $C_8H_9O$ | 48 |
| 91·0547 | 91·0549 | $C_7H_7$ | 30 |

The observed metastable transitions coupled with the data from the Table suggested that all the principal ions were rearranged. This is illustrated in Scheme 4.

The formation of *m/e* 231 from the molecular ion of (IV) revealed a rearrangement, closely related to the one observed in (Ia), *i.e.* the migration of the *ortho*

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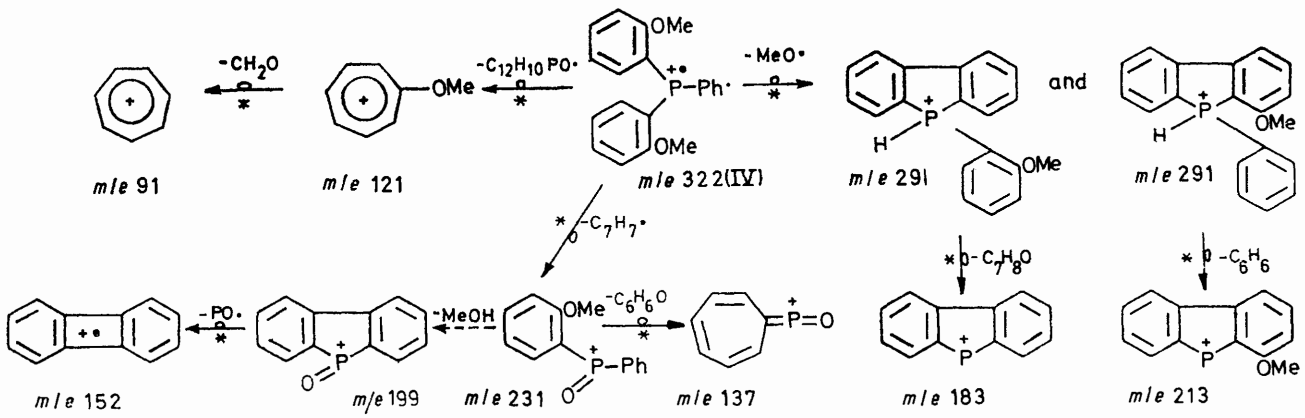
† I. Granoth, unpublished results.

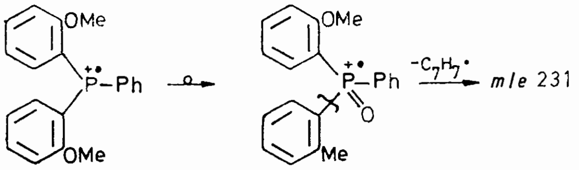
[16] S. Meyerson, H. Drews, and E. K. Fields, *Analyt. Chem.*, 1964, **36**, 1294.

[17] C. S. Barnes and J. L. Occolowitz, *Austral. J. Chem.*, 1963, **16**, 219.



Scheme 4

ether-oxygen to the phosphorus with a simultaneous C–C bond formation to produce the $C_7H_7$ unit:



Another rearrangement involving the migration of a methyl from one ring to another occurred in the molecular ion to enable the formation of *m/e* 121. The latter lost $CH_2O$ giving the tropylium ion, as could be expected.

## EXPERIMENTAL

Low-resolution mass spectra were recorded on an AEI MS9 at 70 eV with source temperature of 170°, using the direct insertion probe. Exact mass measurements were obtained from an MS 902/Picker Nuclear Data acquisition, PDP-8/1 computer at a minimum resolution of 10,000.

10-*Phenylphenoxaphosphine* (Ia).—n-Butyl-lithium (45 ml of 90% hexane solution) was added to a solution of 34·0 g phenyl ether in THF (300 ml) and ether (400 ml) under a dry nitrogen atmosphere. The resulting mixture was refluxed for 5 h after which phenylphosphonous dichloride (27 ml) was added dropwise during 1 h. The mixture was stirred for an additional 10 min, and then water (50 ml) was added dropwise. The organic layer was distilled, and the fraction boiling at 170—180°/0·01 mm was recrystallized from ethanol to yield (Ia) (9·5 g, 17%), m.p. 97—98° (lit.,[18] m.p. 97—98°) (Found: C, 78·2; H, 4·7; P, 11·2. Calc. for $C_{18}H_{13}OP$: C, 78·2; H, 4·7; P, 11·2%).

10-*Phenylphenoxaphosphine* 10-*Oxide* (IIa).—10-Phenylphenoxaphosphine (1·0 g) dissolved in ethanol (10 ml) was treated with 30% $H_2O_2$ solution (1·0 ml) for 10 min. Upon dilution with water, the desired oxide (1·0 g) was precipitated, m.p. 177—178° (lit.,[18] m.p. 176—179°) (Found: C, 73·9; H, 4·6; P, 10·7. Calc. for $C_{18}H_{13}O_2P$: C, 74·0; H, 4·5; P, 10·6%).

10-*Phenylphenoxaphosphine* 10-*Sulphide* (IIIa).—A mixture of (Ia) (2·76 g), sulphur (0·32 g), and benzene (10 ml) was stirred for 15 min, filtered, and diluted with light petroleum to yield the desired sulphide (2·57 g), m.p. 169—170° (Found: C, 69·9; H, 4·3; P, 10·1; S, 10·6. Calc. for $C_{18}H_{13}OPS$: C, 70·1; H, 4·3; P, 10·1; S, 10·4%).

2-*Chloro*-10-*phenylphenoxaphosphine* 10-*Sulphide* (IIIb).—The preparation from (Ib) [3] was carried out as described above for (IIIa); m.p. 140—141° (Found: C, 62·6; H, 3·8. Calc. for $C_{18}H_{12}ClOPS$: C, 63·0; H, 3·5%).

*Bis*-(o-*methoxyphenyl*)*phenylphosphine* (IV).—n-Butyl-lithium (126 ml of 22% hexane solution) was added dropwise in a nitrogen atmosphere to a mixture of anisole (32·4 g), THF (150 ml), and ethyl ether (200 ml). The resulting solution was refluxed for 2 h, and then phenylphosphonous dichloride (17·9 g) was added to it during 1 h. The mixture was refluxed for an additional period of 2 h and was then treated with water (500 ml). A white solid (the desired product) was removed by filtration and later combined with the product (b.p. 140—145°/0·1 mm) obtained from distillation of the organic layer. After recrystallization from ethanol, the product (22·7 g, 70%) melted at 162—163° (Found: C, 74·3; H, 6·1; P, 9·5. Calc. for $C_{20}H_{19}O_2P$: C, 74·5; H, 5·9; P, 9·6%).

*Bis*-(o-*methoxyphenyl*)*phenylphosphine Oxide*.—Bis-(*o*-methoxyphenyl)phenylphosphine (1·61 g), hot ethanol (100 ml), and hydrogen peroxide (10 ml of 30%) were stirred and heated together for 10 min. The mixture was poured into water, and the solid product was removed by filtration and recrystallized from ethanol. The oxide (1·0 g, 59%) melted at 207—209° (Found: C, 71·2; H, 5·6; P, 9·2. Calc. for $C_{20}H_{19}O_3P$: C, 71·0; H, 5·7; P, 9·2%).

Mass spectral data for the six phenoxaphosphines (Ia)—(IIIa) and (Ib)—(IIIb) are deposited with the N.L.L. as Supplementary Publication No. SUP 20334 (3 pp., 1 microfiche).*

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* See notice concerning Supplementary Publication in Notice to Authors No. 7, published in *J. Chem. Soc.* (*A*), issue No. 20, 1970.

[18] J. B. Levy, G. O. Doak, and L. D. Freedman, *J. Org. Chem.*, 1965, **30**, 660.