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## 147. Organic Phosphorus Compounds 52[1]) Preparation and Properties of β-Hydroxyalkyl-phosphonium Salts and Tertiary Phosphine Oxides

by **Ludwig Maier**

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(27. V. 71)

*Summary.* The new, tris-(2-hydroxyalkyl)-(hydroxymethyl)-phosphonium salts: $[(RCHOHCH_2)_3PCH_2OH]Cl$ (I, R = $ClCH_2$; III, R = $CH_3$) are formed in high yield by reaction of tetrakis-(hydroxymethyl)-phosphonium chloride (Tetrakis) with epoxides under basic conditions. Under the same conditions, styrene oxide yields only the disubstituted product, $[(PhCHOHCH_2)_2(CH_2OH)_2P]Cl$. Optimal pH values for the reactions are 8 to 9; at lower pH the conversion is too slow; at a higher pH, oxidative decomposition of the salts occurs. Conversion of the salts to tertiary phosphine oxides $(RCHOHCH_2)_3P{=}O$ (R = $ClCH_2$; $CH_3$) with loss of the hydroxymethyl group is best carried out with chlorine at pH 5 to 7. The yields are usually 60 to 90%.

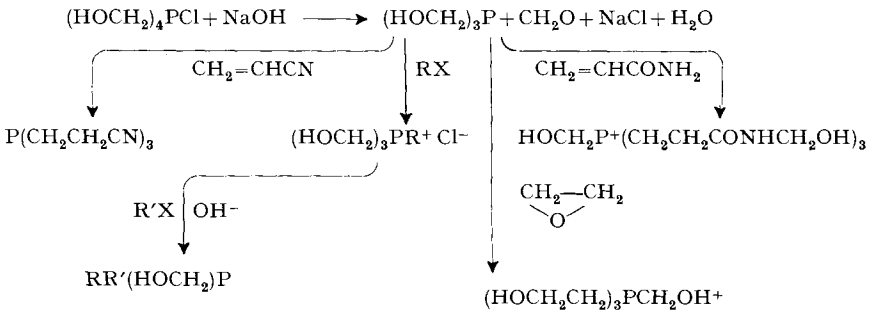
The synthesis of tris-(β-hydroxyethyl)-hydroxymethyl-phosphonium chloride [2] by reaction of tetrakis-(hydroxymethyl)-phosphonium chloride (Tetrakis) with ethylene oxide under basic conditions [2b] has been described.

$$[(HOCH_2)_4P]^+Cl^- + 3\,\underset{\diagdown O \diagup}{CH_2{-}CH_2} \xrightarrow{OH^-} [(HOCH_2CH_2)_3PCH_2OH]^+Cl^- + 3\,CH_2O$$

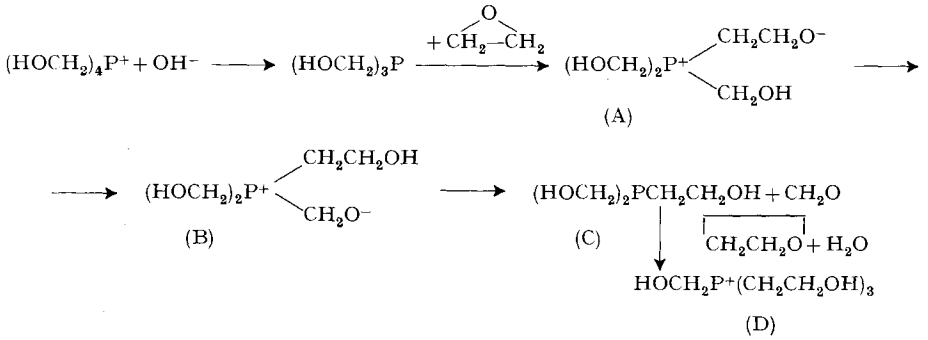
It seemed of interest to explore the scope of this reaction, all the more as only a few examples are known where Tetrakis has undergone reaction resulting in the formation of new carbon-phosphorus bonds [3]. Thus base treatment of Tetrakis

[1]) For n° 51 of this series, see [1].

generates tris-(hydroxymethyl)-phosphine [3] [4] which may give new phosphonium salts after reaction with alkyl halides [4] [5], acrylonitrile [2] [6], acrylamide [2] [7] [8] [9], acrylic acid [2] [8] [10] or epoxides [2] [8] [9], respectively. Since base treatment followed by quaternization may be repeated, starting from Tetrakis tertiary phosphines [3] and new phosphonium salts may be synthesized:




It has recently been shown, that the initial preparation of tris-(hydroxymethyl)-phosphine is unnecessary for effecting the reactions illustrated above .Starting from Tetrakis and the reactants and keeping the reaction mixture basic (pH ~ 8), the end products are obtained in one step [2]. The reaction of Tetrakis with ethylene oxide, in the presence of base, is presumed to involve the following steps:




As before, this sequence also involves tris-(hydroxymethyl)-phosphine as an intermediate. In an independent experiment we could demonstrate that the same end-products are obtained starting from this phosphine. The initially formed zwitter-ion (A) transfers the negative charge to a hydroxymethyl group; the so formed salt (B) is unstable and gives rise to the phosphine (C) and $CH_2O$. Repetition of these steps finally produces the salt D which, after neutralization, is isolated as the chloride. Since it is known that the salts react less readily with base the more the hydroxymethyl groups have been replaced by other groups [4], we suspected that the salt D also contained bis-(hydroxyethyl)-bis-(hydroxymethyl)-phosphonium chloride, $[(HOCH_2\text{-}CH_2)_2\ (HOCH_2)_2P]^+Cl^-$. A detailed $^1H$- and $^{31}$-P-NMR. analysis confirmed this assumption. The $^{31}P$-NMR. spectrum at 40.5 MHz gave the following signals: −31.2 (trace), −31.0 (trace) −30.5 (salt D); −30.2 (trace), and −29.8 ppm (25%). $^1H$-NMR. of salt D in $(CD_3)_2SO/CDCl_3$ (Ref. Tetramethylsilane-capillary):

a) at 3.05 ppm (2*t*, $J_{HH}$ 6.1, $J_{PCH}$ 13 Hz; 5.87H); b) at 4.38 ppm (2*qu*, $J_{HH}$ 6.1, $J_{CHOH}$ 5.2, $J_{PCCH}$ 18.5 Hz; 5.92H); c) at 4.98 ppm (2*d*, $J_{CHOH}$ 7, $J_{PCH}$ 1.5 Hz, 2.51H); d) at 5.95 ppm (*t*, $J_{CHOH}$ 5.2 Hz, 2.56H); and e) at 6.8 ppm (broad, 1.12H).

$$\underset{\text{d b a c e}}{[(HOCH_2CH_2)_3PCH_2OH]^+Cl^-} + \underset{\text{d b a c e}}{[(HOCH_2CH_2)_2P(CH_2OH)_2]^+Cl^-}$$

Tetrakis also reacts with epichlorohydrin and propylene oxide in essentially the same way as with ethylene oxide. As before it was not possible to replace all four hydroxymethyl groups in Tetrakis; even with a large excess of the epoxide only three hydroxymethyl groups could be replaced. The reactions are characterized by moderate exothermicity, an increase in pH and the release of formaldehyde; they are best conducted at pH ca. 8 to 9, maintained by continous addition of dilute acid, since at pH $>$ 10 oxidation to the phosphine oxide occurred at the expense of hydroxymethyl replacement:

$$(HOCH_2)_4P^+ + OH^- + 3\,RCH\!-\!CH_2 \;(\text{O}) \longrightarrow (RCHOHCH_2)_3PCH_2OH^+ + OH^- + 3\,CH_2O$$

$R = CH_2Cl$ (I), $CH_3$ (III)

and at pH $<$ 6, the rate of conversion slowed down considerably.

With styrene oxide only two hydroxymethyl groups could be substituted; at the same time some polymerization seemed to have occurred since the product was a glassy material. No analytical pure sample could be prepared.

Oxidative decomposition of the salts I and III with chlorine at pH 5 to 7 gives high yields of phosphine oxides in which the hydroxymethyl group has been removed.

$$[(RCHOHCH_2)_3PCH_2OH]^+ + Cl_2 \xrightarrow{\text{pH 5–7}} (RCHOHCH_2)_3P{=}O$$

$R = CH_2Cl$ (II); $CH_3$ (IV)

**Experimental**[2]) (with Mr. **A. Hauser**). – 1. $[(\underset{b}{ClCH_2}\underset{c}{CHOH}\underset{e}{CH_2})_3\underset{a}{PCH_2}\underset{d}{OH}\underset{e}{]^+Cl^-}$ (*I*). To 571.3 g (3 moles) of $(HOCH_2)_4PCl$ in 450 ml $H_2O$ a solution of 159 g (2.84 moles) of KOH in 225 ml $H_2O$ is added at 10–15° (ice cooling). Then 832 g (9 moles) of epichlorhydrine are added over 5 h at 20 to 30°, the pH of the mixture being kept at 8–9 by adding 25% hydrochloric acid (340 ml). After 15 h at ambient temperature, the solution is neutralized and evaporated under reduced pressure, then EtOH is added, the precipitated KCl filtered off, and alcohol is distilled from the filtrate. 1121 g (99%) of I, a pale yellow, viscous liquid is obtained; $^{31}$P-chem. shift –32.0 ppm (in $H_2O$): $^1$H-NMR. (in $D_2O$): a) 3.23 ppm (two *d*, (broad) $J_{HH}$ 7, $J_{PCH}$ 13.5 Hz, 6H), b) at 4.2 ppm (two *d*, $J_{HH}$ 5 Hz, 6H), c) at 4.9 ppm (*m*, 3H), d) at 5.15 ppm (*d*, $J_{PCH}$, 1 Hz, 2H), and e) at 5.23 ppm (*s*).

| | | | | | |
|---|---|---|---|---|---|
| $C_{10}H_{21}Cl_4O_4P$ | Calc. | C 31.77 | H 5.60 | Cl 37.51 | P 8.19% |
| (378.08) | Found | ,, 31.88 | ,, 5.68 | ,, 37.38 | ,, 8.08% |

2. $(\underset{b}{ClCH_2}\underset{c}{CHOH}\underset{d}{CH_2}\underset{a}{)_3}P{=}O$ (*II*). To 33.5 g (0.0886 mole) of I, dissolved in 170 ml $H_2O$, hydrochloric acid is added to adjust the pH to 5–7. Over a period of 1 h 13.9 g (0.195 mole) of chlorine are bubbled into the solution whereby the temperature is kept at 20° and the pH at 5–7. The mixture is then neutralized, and, after removing traces of unchanged salt I by means of an ion exchanger ($Na^+$-form), the solution is neutralized, evaporated under reduced pressure, the residue dissolved in EtOH, the precipitated NaCl filtered off and alcohol distilled from the filtrate. 19 g (65.5%) of II, a pale yellow, viscous liquid, is obtained. $^{31}$P-chem. shift (in $H_2O$): $-51.7 \pm 1$ ppm.

[2]) The microanalyses were carried out by *A. Manser*, ETH Zürich. The $^{31}$P-NMR.-spectra were effected at 24.298 MHz with 85% $H_3PO_4$ as external reference. The $^1$N-NMR. were effected at 60 MHz with $Me_4Si$ as reference.

$^1$H-NMR. (in $D_2O$): a) at 2.85 ppm (*m*, 6H), b) at 4.2 ppm (broad *d*, 6H), c) at 4.75 ppm (*m*, 3.3H), and d) at 5.22 ppm (*s*).

$C_9H_{18}Cl_3O_4P$ (327.6) Calc. C 32.99 H 5.54 Cl 32.47% Found C 32.85 H 5.62 Cl 32.32%

3. $[(\overset{a}{CH_3}\overset{c}{CHOH}\overset{e}{CH_2})_3\overset{b}{P}\overset{d}{CH_2}\overset{e}{OH}]^+Cl^-$ (*III*). From 190.5 g (1 mole) of $(HOCH_2)_4PCl$ in 150 ml $H_2O$, 53 g KOH in 150 ml $H_2O$, pH 8, and 191 g (3.3 moles) propylene oxide as in 1, 247 g (90.1%) of III, a colorless, viscous oil, is obtained. $^{31}$P-chem. shift (in $H_2O$) –28.6 ppm. $^1$H-NMR. (in $D_2O$): a) at 1.85 ppm (two *t*, $J_{HH}$ 7, $J_{PCCCH}$ 2.5 Hz, 9H), b) at 3.1 (*m*, 5.95 H), c) at 4.75 ppm (*m*, 3.05 H), d) at 5.10 ppm (*d*, $J_{PCH}$ 1.8 Hz, 2.2 H), and e) at 5.25 ppm (*s*).

$C_{10}H_{24}ClO_4P$ (274.7) Calc. C 43.72 H 8.80 Cl 12.91% Found C 43.64 H 8.76 Cl 12.92%

4. $(\overset{a}{CH_3}\overset{c}{CHOH}\overset{d}{CH_2})_3\overset{b}{P}{=}O$ (*IV*). From 11.1 g (0.0404 mole) III, 50 ml $H_2O$, 6.3 g (0.089 mole) chlorine, pH kept at 4–7; procedure and isolation as in 2 gives 8.5 g (93.6%) of IV, a colorless viscous liquid, $^{31}$P-chem. shift (in $H_2O$) –51.0 ppm: $^1$H-NMR. (in $D_2O$): a) at 1.8 ppm ($J_{HH}$ 6, $J_{PCH}$ 1.4 Hz, 9H), b) at 2.65 ppm (*m*, 6H), c) 4.55 ppm (*m*, 3.4 H) ,and d) at 5.27 ppm (*s*).

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# 148. Microcalorimetric Measurements with the Valinomycin - Potassium Iodide Complex[1])

Preliminary Communication[2])


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(18. V. 71)


*Zusammenfassung.* Die Mikrokalorimetrie wurde erstmals zur Bestimmung von Assoziationskonstante, Reaktionsenthalpie, freier Reaktionsenergie und Reaktionsentropie der Komplexbildung zwischen Kaliumjodid und Valinomycin in Äthanol verwendet. Eine konstante Konzentration von Valinomycin ($10^{-4}$ M) wurde mit verschiedenen Konzentrationen von Kaliumjodid ($10^{-5}$ bis $10^{-3}$ M) versetzt. Die Enthalpieänderung (Grössenordnung 0,5 bis 5,0 mcal) wurde als Titrationsparameter benützt. Die Auswertung der Sättigungskurve nach *Klopfenstein* [3] ergab


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[1]) Part of the thesis of *H. M.*; discussed at the 11th European Peptide Symposium, Vienna, April 29, 1971.

[2]) A full paper will be submitted to Helv.