Anomalous Reactivity of Diphenylhydroxymethylphosphine Oxide in the Synthesis of a Phosphorylated Ether by Oxa-Michael Reaction

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Abstract: Vinylic phosphorus compounds were found to react as Michael olefins with alcohols in basic catalytic conditions. Several phosphorylated polyethers were obtained in such a way. In analogous conditions, the hydroxymethylphosphine oxide used as alcoholic reagent looses formaldehyde leading to 1,2-diphosphorus compound formation. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Five percents of the total amount of the radioactive wastes produced by the nuclear industry are constituted by long life radionuclides. These radioactive nuclides are particularly minor actinides (neptunium, americium and curium) and fission products (like strontium and cesium). In order to reprocessing this part of the wastes, we have developed, in previous investigations[1], specific complexing agents for a very efficient separation process using supported liquid membrane (SLM). Still for this purpose, we are reporting now the synthesis of new (O)PCCO bridged ethers by Michael type reaction.

Maier[2] has shown that the synthesis of ethers by Williamson reaction between alkoxide and β-halogenated phosphine oxide occurs indeed through a β–elimination reaction in the first step. Then the second step is the *in situ* reaction of the alkoxide with the new generated vinylphosphine oxide in an oxa-Michael reaction. Consequently, Tsvetkov *et al*[3] used directly diethyl vinylphosphonate **2** with polyethyleneglycol to obtain ether compounds.

We have generalized this method by reacting a vinylic phosphorus compound with an alcohol in basic catalytic conditions. Diethyl 5-hydroxy-3-oxapentylphosphonate **3** was synthesized by reaction of diethyl vinylphosphonate **2** (1 eq) with an excess of ethyleneglycol **1** (7 eq) and catalytic amount of KOH (0,3 eq)[4] : **3** is isolated in 61% yield[5] (Scheme 1). In these conditions, less than 5% of the bisphosphonate resulting of a double addition to **1** is formed.
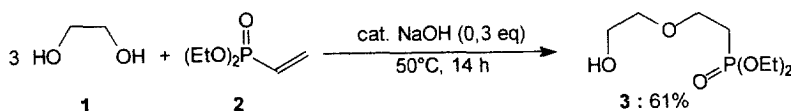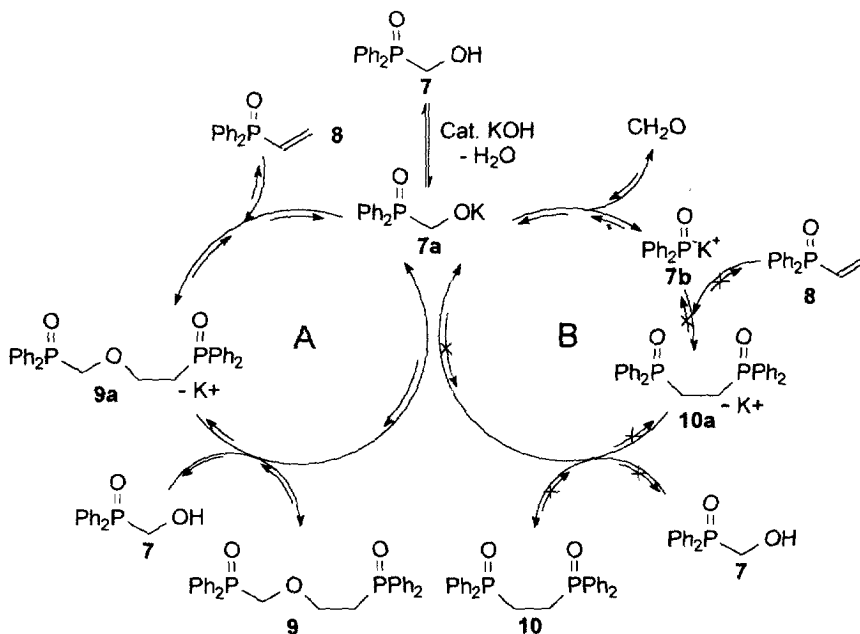

Scheme 1

Similarly, **2** reacts with triethanolamine **4** to give tris(5-O,O'-diethylphosphono-3-oxapentyl)amine **5** in 85% yield, by successive addition reactions. Subsequent hydrolysis in acidic media (HCl 35%) leads to trisphosphonic acid **6** in quantitative yield[6] (see Scheme 2).
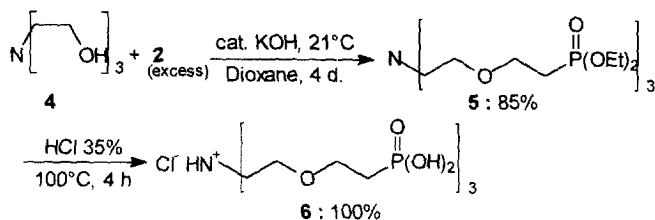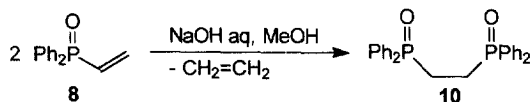

Scheme 2

In the same way, in order to introduce simultaneously a second phosphoryl group and the ether function, we used hydroxymethylphosphine oxides as alcoholic compounds for oxa-Michael reaction. Then, the reaction between diphenylhydroxymethylphosphine oxide **7** and diphenylvinylphosphine oxide **8** also gives the ether compound **9**. However, compound **9** cannot be isolated in yield higher than 46%[7]. Indeed, all our attempts to improve the yields, either by increasing the temperature or changing the base quantity, lead to the formation of 1,2-bis(diphenylphosphino)ethane dioxide **10** as the major or even single product. We manage to establish the formation mechanism of **9** and **10** (see Scheme 3) : the catalytic cycle *A* represents the expected reaction of alkoxide **7a** with **8** to give in the first step the carbanion **9a**. In a second step, acid-base reaction of **9a** and **7** leads to the ether product **9**. The complete reversibility of the catalytic cycle *A* is demonstrated by addition of an excess of NaOH (3 eq) to **9**, which is quantitatively transformed into **10** in one hour.
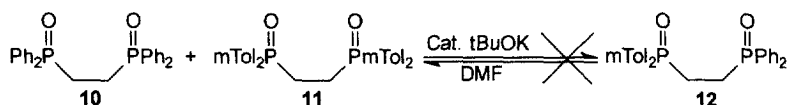

Scheme 3

For the formation of **10**, we exclude the exclusive transformation of **8** observed by Postle *et al*[8] (see Scheme 4), because we should obtain two phosphorus end products by this way (**10** and **7**). In our mechanism according to the catalytic cycle **B**, the first step is a retro-formylation reaction previously reported for the tris(hydroxymethyl)phosphine[9] and hydroxymethylphosphonium salts[10]. Hence, we obtain potassium diphenylphosphinate **7b** which reacts as a concurrent nucleophile with **8** to give carbanion **10a**, followed by acid-base reaction leading to **10**.

Scheme 4

Moreover, we can explain the preponderant formation of the diphosphine dioxide **10** in more drastic conditions, by the irreversibility of some reactions in the catalytic cycle **B**. This hypothesis is verified with the following experiment : when **10** and **11** are mixed with *t*BuOK, phosphine oxide carbanions are formed, without the formation of dissymmetric diphosphine dioxide **12** through retro-Michael reaction (Scheme 5). Therefore, the reaction of **7b** with **8** to give **10a** is irreversible[11].

Scheme 5

In conclusion, the addition of alcohol to vinylphosphorus compound with base catalyst, appears to be a general pathway to obtain (O)PCCO ethers in good yields. However, hydroxymethylphosphine oxides can present anomalous reactivity with the lost of formaldehyde. Then, the use of drastic conditions could provide a new way to synthesize symmetric or dissymmetric 1,2-diphosphine dioxide compounds using stable precursors.

References and Notes

(1) Dozol, J.F.; Rouquette, H.; Cristau, H.J.; Mouchet, P.; *French Patent* n°9315295 **1993**.
      Cristau, H.J.; Mouchet, P.; Dozol, J.F.; Rouquette, H.; *Heteroatom Chemistry* **1995**, *6*, 533-544.
(2) Maier, L. ; *Phosphorus* **1972**, *1*, 245-248.
(3) Turanov, A.N. ; Baulin, V.E. ; Kharitonov, A.V. ; Tsvetkov, E.N. ; *Russ. J. Inorg. Chem.* **1994**, *39*, 1330-1335.
(4) Typical procedure for the synthesis of (O)PCCO compounds : A solution of 15 ml of dioxane, 1 g of alcohol (1eq), 1 or 3 eq of the vinylic phosphorus compound[12] and 0,1 eq of KOH are stirred for 4 days at room temperature. After addition of water, pH is adjusted to 7 by 1 N HCl, and the reaction mixture is extracted by dichloromethane and dried on Na_2SO_4. The residue is chromatographied on silica gel (AcOEt/MeOH eluent).
(5) Spectroscopic data for diethyl 5-hydroxy-3-oxapentylphosphonate **3** : ^{31}P NMR : δ = 30.17 (s, P). ^{1}H NMR : δ = 1.23 (t, 6H, $^{3}J_{HH}$= 7.1 Hz, CH_3) ; 2.01 (td, 2H, $^{3}J_{HH}$= 6.9 Hz, $^{3}J_{PH}$= 18.2 Hz, $^{1}CH_2$) ; 3.45-3.74 (m, 6H, $^{2,4,5}CH_2$) ; 3.94-4.09 (m, 4H, POC$\underline{H}_2$).

^{13}C NMR : δ = 16.31 (d, $^3J_{PC}$= 6.1 Hz, CH$_3$) ; 26.84 (d, $^1J_{PC}$= 140.8 Hz, ^{1}CH$_2$) ; 61.15 (s, ^{5}CH$_2$) ; 61.67 (d, $^2J_{PC}$= 6.4 Hz, POCH$_2$) ; 64.47 (d, $^2J_{PC}$= 3.8 Hz, ^{2}CH$_2$) ; 72.11 (s, ^{4}CH$_2$). IR (Film NaCl) : 3390 (s), 2979 (m), 2928 (m), 2905 (m), 2870 (m), 1250 (m), 1224 (s), 1120 (s), 1099 (m), 1054 (vs), 1028 (vs), 993 (m), 962 (s) cm^{-1}. MS (FAB$^+$, NBA) : m/z = 227 (100) MH$^+$, 199 (5) (M - CH$_2$=CH$_2$)$^-$, 109 (20) H$_2$O$_3$PCH$_2$CH$_2$$^+$.

(6) Spectroscopic data for tris(5-O,O'-diethylphosphono-3-oxapentyl)amine **5** : ^{31}P NMR : δ = 28.96 (s). ^{1}H NMR : δ = 1.17 (t, 18H, $^3J_{HH}$= 7.1 Hz, CH$_3$), 1.94 (td, 6H, $^3J_{HH}$= 7.6 Hz, $^2J_{PH}$= 18.7 Hz, ^{5}CH$_2$), 2.61 (t, 6H, $^3J_{HH}$= 6.1 Hz, ^{1}CH$_2$), 3.35 (t, 6H, $^3J_{HH}$= 6.1 Hz, ^{2}CH$_2$), 3.51 (td, 6H, $^3J_{HH}$= 7.6 Hz, $^3J_{PH}$= 10.8 Hz, ^{4}CH$_2$), 3.95 (m, 12H, POCH$_2$). ^{13}C NMR : δ = 16.30 (d, $^3J_{PC}$= 6.0 Hz, CH$_3$), 26.88 (d, $^1J_{PC}$= 139.2 Hz, ^{5}CH$_2$), 54.39 (s, ^{1}CH$_2$), 61.42 (d, $^3J_{PC}$= 6.3 Hz, POCH$_2$), 64.80 (s, ^{2}CH$_2$) ; 69.28 (s, ^{4}CH$_2$). IR (Film, NaCl) : 2976, 2925, 2900, 2866, 1733, 1476, 1470, 1441, 1390, 1367, 1244, 1162, 1111, 1098, 1040, 99, 960, 792, 731, 700 cm^{-1}. MS (FAB$^+$, NBA) : m/z = 642 (100) MH$^+$, 446 (50), 238 (40), 109 (55). Spectroscopic data for tris(5-phosphono-3-oxapentyl)ammonium chloride **6** : ^{31}P NMR *(D$_2$O)* : δ = 27.25 (s). ^{1}H NMR *(D$_2$O)* : δ = 2.12 (td, $^3J_{HH}$= 6.8 Hz, $^2J_{PH}$= 18.0 Hz, ^{5}CH$_2$) ; 3.52 (m, ^{1}CH$_2$) ; 3.69-3.90 (m, ^{2}CH$_2$ and ^{4}CH$_2$). ^{13}C NMR *(D$_2$O)* : δ = 30.06 (d, $^1J_{PC}$= 135.0 Hz, ^{5}CH$_2$) ; 55.98 (s, ^{1}CH$_2$) ; 66.61 (s, ^{2}CH$_2$) ; 68.03 (d, $^2J_{PC}$= 3.5 Hz, ^{4}CH$_2$).

(7) Spectroscopic data for 1,4-bis(diphenylphosphino)-2-oxabutane dioxide **9** : crystalline solid ; mp 185-187°C. ^{31}P NMR : δ = 27.6 (s, PCH$_2$) ; 29.42 (s, PCH$_2$CH$_2$). ^{1}H NMR : δ = 2.56 (m, 2H, $^2J_{PH}$= -11.7 Hz, $^3J_{HH}$= 7.8 Hz, PC**H**$_2$ CH$_2$) ; 3.85 (td, 2H, $^3J_{PH}$= 8.1 Hz, $^3J_{HH}$= 7.8 Hz, PCH$_2$ C**H**$_2$) ; 4.16 (d, 2H, $^2J_{PH}$= 6.32 Hz, PC**H**$_2$O) ; 7.34-7.51 and 7.60-7.74 (2 m, 20H, aromatic CH). ^{13}C NMR : δ = 30.6 (d, $^1J_{PC}$= 70.3 Hz, P**C**H$_2$CH$_2$) ; 67.7 (d, $^2J_{PC}$= 11.6 Hz, PCH$_2$**C**H$_2$) ; 69.3 (d, $^1J_{PC}$= 87.5 Hz, P**C**H$_2$O) ; 128.5 (d, $^2J_{PC}$= 7.3 Hz, CH) ; 128.6 (d, $^2J_{PC}$= 7.3 Hz) ; 130.62 (d, $^3J_{PC}$= 9.6 Hz, CH) ; 130.81 (d, $^1J_{PC}$= 88.5 Hz, C) ; 131.39 (d, $^3J_{PC}$= 9.5 Hz, CH) ; 131.9 (d, $^4J_{PC}$= 2.8 Hz, CH) ; 132.15 (d, $^4J_{PC}$= 2.7 Hz, CH) ; 132.8 (d, $^1J_{PC}$= 88.9 Hz, C). IR *(KBr)* : 3050 (m), 2895 (m), 1435 (s), 1390 (m), 1195 (s), 1180 (vs), 1161 (m), 1120 (s), 1095 (s), 1071 (m), 996 (m), 922 (m), 878 (m), 780 (m), 768 (m), 748 (s), 717 (s), 693 (vs), 558 (vs), 509 (vs), 450 (m) cm^{-1}. MS (FAB$^+$, NBA) : m/z = 461 (100) MH$^-$, 259 (10) [M-Ph$_2$PO]$^+$, 229 (20) Ph$_2$P(O)CH$_2$CH$_2$$^+$, 201 (60) Ph$_2PO^-$. C$_{27}H_{26}O_3P_2$ (460,4) : Calc. C, 70.4 ; H, 5.7. Found C, 70.2 ; H, C5.9.

(8) Postle, S.R. ; Whitham, G.H. : *J. Chem. Soc, Perkin I* **1977**, 2084-2088.

(9) Valetdinov, R.K. ; Kuznetsov, E.V. ; Komissarova, S.L. ; *J. Gen. Chem. SSSR* **1969**, *36*, 1708-1710.

(10) Petrov, K.A. ; Parshina, V.A. ; Luzanova, M.B. ; *J.Gen. Chem. SSSR* **1962**, *32*, 542-545.

Ellis, J.W. ; Harrison, K.N. ; Hoye, P.A.T. ; Orpen, A.G. ; Pringle, P.G. ; Smith, M.B. ; *Inorg. Chem.* **1992**, *31*, 3026-3033.

(11) 0.4 g of **10** and **11** are mixed in 5 mL of DMF. 0.1 g of *t*BuOK is added and the solution becomes yellow according to the formation of the phosphine oxides carbanions. The evolution of the reaction is carried out by ^{31}P NMR.

(12) diethylvinyl phosphonate and diphenylvinylphosphine oxide were prepared according to the literature : Collins, D.J. ; Rowley, L.E. ; Swan, J.M. ; *Aust. J. Chem.* **1974**, *27*, 841-851 ; Hellmann, H. ; Bader, J. ; Birkner, H. ; Schumacher, O. ; *J. Liebigs Ann. Chem.* **1962**, *659*, 49-63 ; Kosolapoff, G. ; *J. Am. Chem. Soc.* **1948**, *70*, 1971-1972.