

TETRAHEDRON LETTERS

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 investigations¹, 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.

Maier² 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 $(0,3 \text{ eq})^4$: **3** is isolated in 61% yield⁵ (Scheme 1). In these conditions, less than 5% of the bisphosphonate resulting of a double addition to **1** is formed.



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 yield⁶ (see 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.



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)phosphine⁹ and hydroxymethylphosphonium salts¹⁰. 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.



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 irreversible¹¹.



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.

Acknowledgments

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References and Notes

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- (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 compound¹² 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 Na₂SO₄. The residue is chromatographied on silica gel (AcOEt/MeOH eluent).
- (5) Spectroscopic data for diethyl 5-hydroxy-3-oxapentylphosphonate $3 : {}^{31}P$ NMR : $\delta = 30.17$ (s, P). ${}^{1}H$ NMR : $\delta = 1.23$ (t, 6H, ${}^{3}J_{HH} = 7.1$ Hz, CH₃) ; 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, ${}^{24.5}CH_2$) ; 3.94-4.09 (m, 4H, POCH₂).

¹³C NMR : $\delta = 16.31$ (d, ³ $J_{PC}= 6.1$ Hz, CH₃) ; 26.84 (d, ¹ $J_{PC}= 140.8$ Hz, ¹CH₂) ; 61.15 (s, ⁵CH₂) ; 61.67 (d, ² $J_{PC}= 6.4$ Hz, POCH₂) ; 64.47 (d, ² $J_{PC}= 3.8$ Hz, ²CH₂) ; 72.11 (s, ⁴CH₂). IR (Film NaCl) : 3390 (s), 2979 (m), 2928 (m), 2905 (m), 2870 (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 - CH₂=CH₂)⁺, 109 (20) H₂O₃PCH₂CH₂⁺.

- (6) Spectroscopic data for tris(5-O,O'-diethylphosphono-3-oxapentyl)amine $5:{}^{31}P$ NMR : $\delta = 28.96$ (s). ${}^{1}H$ NMR : $\delta = 1.17$ (t, 18H, ${}^{3}J_{HH} = 7.1$ Hz, CH₃), 1.94 (td, 6H, ${}^{3}J_{HH} = 7.6$ Hz, ${}^{2}J_{PH} = 18.7$ Hz, ${}^{5}CH_{2}$), 2.61 (t, 6H, ${}^{3}J_{HH} = 6.1$ Hz, ${}^{1}CH_{2}$), 3.35 (t, 6H, ${}^{3}J_{HH} = 6.1$ Hz, ${}^{2}CH_{2}$), 3.51 (td, 6H, ${}^{3}J_{HH} = 7.6$ Hz, ${}^{3}J_{PH} = 10.8$ Hz, ${}^{4}CH_{2}$), 3.95 (m, 12H, POCH₂). ${}^{13}C$ NMR : $\delta = 16.30$ (d, ${}^{3}J_{PC} = 6.0$ Hz, CH₃), 26.88 (d, ${}^{1}J_{PC} = 139.2$ Hz, ${}^{5}CH_{2}$), 54.39 (s, ${}^{1}CH_{2}$), 61.42 (d, ${}^{3}J_{PC} = 6.3$ Hz, POCH₂), 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_2O) : $\delta = 27.25$ (s). ${}^{1}H$ NMR (D_2O) : $\delta = 2.12$ (td, ${}^{3}J_{HH} = 6.8$ Hz, ${}^{2}J_{PH} = 18.0$ 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_2O) : $\delta = 30.06$ (d, ${}^{1}J_{PC} = 135.0$ Hz, ${}^{5}CH_{2}$) ; 55.98 (s, ${}^{1}CH_{2}$) ; 66.61 (s, ${}^{2}CH_{2}$) ; 68.03 (d, ${}^{2}J_{PC} = 3.5$ Hz, ${}^{4}CH_{2}$).
- (7) Spectroscopic data for 1,4-bis(diphenylphosphino)-2-oxabutane dioxide 9 : crystalline solid ; mp 185-187°C. ³¹P NMR : $\delta = 27.6$ (s, PCH₂) ; 29.42 (s, PCH₂CH₂). ¹H NMR : $\delta = 2.56$ (m, 2H, ² $J_{PH}^{=}$ -11.7 Hz, ³ $J_{HH}^{=}$ 7.8 Hz, PCH₂ CH₂) ; 3.85 (td, 2H, ³ $J_{PH}^{=}$ 8.1 Hz, ³ $J_{HH}^{=}$ 7.8 Hz, PCH₂ CH₂) ; 4.16 (d, 2H, ² $J_{PH}^{=}$ 6.32 Hz, PCH₂O) ; 7.34-7.51 and 7.60-7.74 (2 m, 20H, aromatic CH). ¹³C NMR : $\delta = 30.6$ (d, ¹ $J_{PC}^{=}$ 70.3 Hz, PCH₂CH₂) ; 67.7 (d, ² $J_{PC}^{=}$ 11.6 Hz, PCH₂CH₂) ; 69.3 (d, ¹ $J_{PC}^{=}$ 87.5 Hz, PCH₂O) ; 128.5 (d, ² $J_{PC}^{=}$ 7.3 Hz, CH) ; 128.6 (d, ² $J_{PC}^{=}$ 7.3 Hz) ; 130.62 (d, ³ $J_{PC}^{=}$ 9.6 Hz, CH) ; 130.81 (d, ¹ $J_{PC}^{=}$ 88.5 Hz, C) ; 131.39 (d, ³ $J_{PC}^{=}$ 9.5 Hz, CH) ; 131.9 (d, ⁴ $J_{PC}^{=}$ 2.8 Hz, CH) ; 132.15 (d, ⁴ $J_{PC}^{=}$ 2.7 Hz, CH) ; 132.8 (d, ¹ $J_{PC}^{=}$ 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-Ph₂PO]⁺, 229 (20) Ph₂P(O)CH₂CH₂⁺, 201 (60) Ph₂PO⁺. C₂₇H₂₆O₃P₂ (460,4) : Calc. C, 70.4 ; H, 5.7. Found C, 70.2 ; H, C5.9.
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 (11)0.4 g of 10 and 11 are mixed in 5 mL of DMF. 0.1 g of *tBuOK* 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 ³¹P 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.