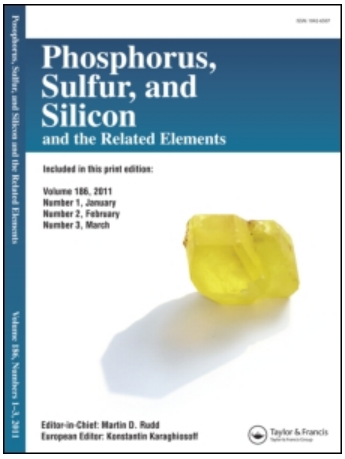

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Communication

REACTIVITY OF PHOSPHONIC KETENE DITHIOACETALS TOWARDS NUCLEOPHILES

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The reaction of phosphonic ketene dithioacetals with two types of nucleophiles is described: alkoxides and Grignard reagents in the presence of transition metal catalysts.

Key words: Phosphonates; ketenedithioacetals; ketene acetals; nucleophilic substitution; Grignard reagents

Syntheses of phosphonic ketene dithioacetals were recently described in three different papers.[1,2,3] During the study of their reactivity towards amino-nucleophiles, we observed, with ethanol as solvent, the substitution of the methylthio group by an ethoxy group. It is known that the reaction of a ketene dithioacetal with an amino-alcohol leads to the substitution of both sulfur atoms by nitrogen and oxygen atoms, yielding a cyclic O,N-acetal.[4] We report here the substitution of sulfur by alkoxides in diphosphonic ketene dithioacetals. Phosphonic ketene dithioacetal **1** reacts with sodium ethoxide to yield ketene acetal **2**, it also reacts with disodium salt **3** of ethylene glycol and with the disodium salt **4** of 2-mercaptoethanol, yielding sulfur substitution products **5** and **6** (Scheme I).

Grignard reagents can, in the presence of a transition metal catalyst, substitute the sulfur atom in vinyl sulfides[5] and in ketene dithioacetals.[6] We report here the substitution of the sulfur atoms in diphosphonic ketene dithioacetals by methyl and aryl groups. Phosphonic ketene dithioacetal **1** reacts, in the presence of copper (I) iodide, with methylmagnesium iodide and with phenylmagnesium bromide to yield gem dialkylation products **7** (16%) and **8** (Scheme II). The trimethylation product (≈40%) was formed while using methylmagnesium iodide. A similar phenomenon was observed by Corey and Chen in the reaction of organocuprates with ketene α-oxodithioacetals.[7] The trialkylation is not observed with phenylmagnesium bromide probably because of the size of the nucleophile.

In all cases the yields are not optimized and the phosphonates are partially degraded during the chromatography on silica.

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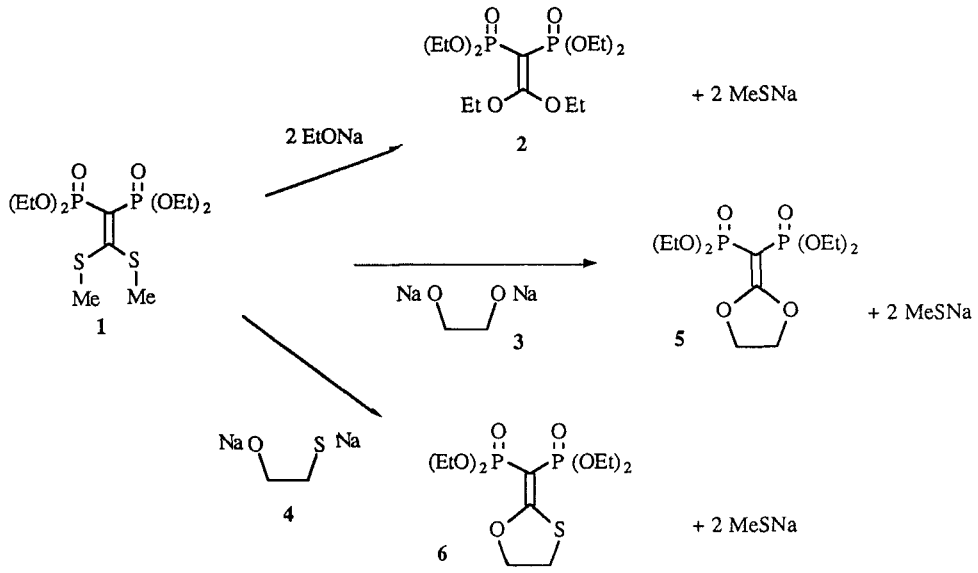
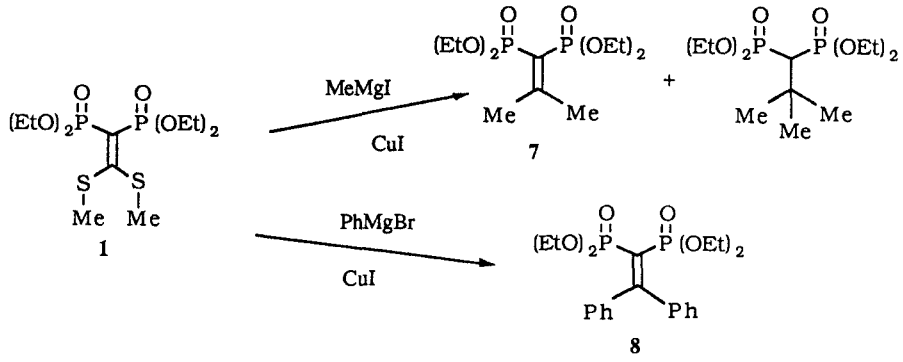


SCHEME I Reaction of phosphonic ketene dithioacetals with oxygen and sulfur nucleophiles.



SCHEME II Reaction of phosphonic ketene dithioacetals with Grignard Reagents.

EXPERIMENTAL

Infrared spectra (in cm^{-1}) were recorded in KBr or between NaCl plates on a Perkin Elmer 684 IR spectrophotometer. Proton NMR spectra (PMR) were recorded in ppm downfield from internal Me_4Si on a Varian EM 360 instrument (60 MHz). ^{13}C NMR spectra were recorded in ppm downfield from internal Me_4Si on a Brucker WP 60, as were the ^{31}P NMR spectra, in ppm down field from external H_3PO_4. Mass spectra (MS) were recorded on a Nermag R10-10H spectrometer. Boiling points (Bp) are in °C, with the distillation pressure in brackets in mbars. Synthesis of tetraethyl 2,2-di(methylthio)ethenediylidenediphosphonate **1** was described previously.[2]

Tetraethyl 2,2-diethyloxyethenediyldiphosphonate (**2**). *Typical procedure.* Sodium (0.25 g, 11 mmol) was placed in a 100 ml flask with 30 ml dry THF. Ethanol (0.66 ml, 11 mmol) is added. The mixture is heated at refluxing temperature during 2 h. The phosphonic ketene dithioacetal **1** (1.96 g, 5 mmol) is added and the mixture heated at refluxing temperature for 48 h. After cooling, 150 ml ether were added, the mixture is filtered and the solvent is distilled. The product is obtained by chromatogra-

phy on a silica-gel column (eluent CH_2Cl_2/MeOH = 95/5). It is a colourless liquid. The yield is 62% (1.2 g).

^1H NMR ($CDCl_3$) δ: 1.3 (t, 12 H, ^3J = 7 Hz, CH_3), 3.9–4.5 (m, 8 H, CH_2).

^{13}C NMR ($CDCl_3$) δ: 14.0 (C—O—C—$\underline{C}H_3$), 16.3 (t, P—O—C—$\underline{C}H_3$), 48.1 (t, $^1J_{C—P}$ = 127 Hz, P—C—P), 62.6 (t, $^5J_{C—P}$ = 3 Hz, C—O—$\underline{C}H_2$), 63.4 (P—O—CH_2), 163.5 (t, $^4J_{C—P}$ = 7 Hz, P—C=$\underline{C}$).

^{31}P NMR ($CDCl_3$) δ: 13.2.

Tetraethyl (1,3-dioxolan-2-ylidene)methylenediphosphonate (**5**). It is prepared with the same procedure as **2**, from 2-hydroxyethanol (0.28 ml, 5 mmol) instead of ethanol and the same quantities of the other reactants. It is a colourless liquid, the yield is 26% (0.46 g).

^1H NMR ($CDCl_3$) δ: 1.25 (t, J = 7 Hz, 12 H, CH_3), 2.6 (t, J = 7 Hz, 4 H, CH_2—CH_2), 4.1 (dq, J^1 = J^2 = 7 Hz, 8 H, CH_2).

^{13}C NMR ($CDCl_3$) δ: 16.4 (t, P—O—C—$\underline{C}H_3$), 48.2 (t, $^1J_{C—P}$ = 128 Hz, P—C—P), 63.4 (P—O—CH_2), 65.0 (C—O—$\underline{C}H_2$), 163.6 (t, $^4J_{C—P}$ = 6 Hz, P—C=$\underline{C}$).

^{31}P NMR ($CDCl_3$) δ: 13.0.

Tetraethyl (1-oxa-3-thiolan-2-ylidene)methylenediphosphonate (**6**). It is prepared with the same procedure as **2**, from 2-mercaptoethanol (0.35 ml, 5 mmol) instead of ethanol and the same quantities of the other reactants. It is a colourless liquid, the yield is 46% (0.87 g).

^1H NMR ($CDCl_3$) δ: 1.3 (t, J = 7 Hz, 12 H, CH_3), 2.45 (t, J = 8 Hz, 2 H, S—CH_2), 4.0 (t, J = 8 Hz, 2 H, O—CH_2), 4.15 dq, J^1 = J^2 = 7 Hz, 12 H, P—O—CH_2).

^{31}P NMR ($CDCl_3$) δ: 28.0 (d, 78 Hz), 33.0 (d, 78 Hz).

Tetraethyl 2,2-dimethylethenediyldiphosphonate (**7**). Phosphonic ketene dithioacetal **1** (5 mmol, 1.96 g) is placed in a 50 ml round bottomed flask with CuI (0.5 mmol, 95 mg) and 20 ml toluene under nitrogen atmosphere. The flask is cooled with ice. 15 ml of methyl magnesium iodide solution in ether (1 M, 15 mmol) is added within 30 Mn—the solution is prepared using activated[8] magnesium turnings (50 mmol, 1.22 g) and iodomethane (50 mmol, 3.1 ml) in dry ether. The mixture becomes clear and then dark. The flask is left at room temperature and agitated for 15 h under nitrogen. Methanol is added and the mixture is concentrated under reduced pressure and dissolved in 25 ml methylene chloride. The mixture is filtered and the solvent evaporated. The product, a colourless liquid, is obtained by distillation, the yield is 16% (0.26 g). The trimethylation product, identified by its mass spectrum, is found as a residue (0.69 g, 40%) in the distillation flask, together with degradation products (≈0.70 g),

Bp: 120 (0.01).

^1H NMR ($CDCl_3$) δ: 1.25 (s, 6 H, P—C=C—CH_3), 1.35 (t, J = 7 Hz, 12 H, P—O—C—CH_3), 4.15 (dq, J^1 = J^2 = 7 Hz, 8 H, P—O—CH_2).

^{13}C NMR ($CDCl_3$) δ: 16.5 (P—O—C—$\underline{C}H_3$), 30.7 (t, $^3J_{P—C}$ = 128 Hz, P—C—P), 138 (t, $^2J_{P—C}$ = 8 Hz, P—C=C—$\underline{C}H_3$).

^{31}P NMR ($CDCl_3$) δ: 23.3.

MS m/z (%): 328 (M^+, 36), 287 (71), 232 (100), 215 (56), 204 (61), 193 (88).

Tetraethyl 2,2-diphenylethenediyldiphosphonate (**8**). It is prepared with the same procedure as **7**, from phosphonic ketenedithioacetal **1** (5 mmol, 1.96 g) and a solution of phenylmagnesium bromide in dry THF (25 ml, 0.5 M, 12.5 mmol), in the presence of CuI (0.5 mmol, 95 mg) under nitrogen, at 0°C. The copper complex obtained is dissociated by dissolution in THF and washing with 5 ml of KCN saturated solution in water. The organic phase is dried over magnesium sulfate and the solvent is distilled under reduced pressure. The product is a brown solid, the yield is 33% (0.74 g).

^1H NMR ($CDCl_3$) δ: 1.3 (t, J = 7 Hz, 12 H, P—O—C—CH_3), 4.1 (dq, J^1 = J^2 = 7 Hz, 8 H, P—O—CH_2), 7.1–7.7 (m, 10 H, Ar).

^{13}C NMR ($CDCl_3$) δ: 16.3 (t, P—O—C—$\underline{C}H_3$), 62.6 (P—O—CH_2), 127.2, 127.3, 128.9, 141.4 (Ar), 151.6 (P—C=$\underline{C}$).

^{31}P NMR ($CDCl_3$) δ: 24.05.

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