Reaction of Dimethyl Phosphonate with Ketene Dimethyl Dithioacetal Derivatives. An Alternative Method to Prepare *s*-Alkylphosphonates

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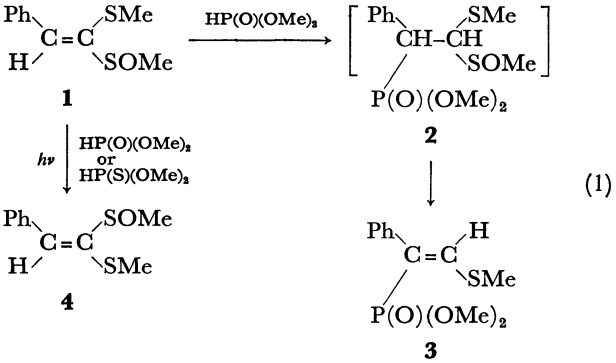
Reaction of dimethyl phosphonate with phenylketene dimethyl dithioacetal derivatives have been investigated to prepare *s*-alkylphosphonates. The addition reactions of phosphonate were accelerated in dithioacetal derivatives in the following order: –SMe<–SOMe≪–SO_2Me. The reaction of β,β-bis(methylsulfonyl)styrene (**7**) with dimethyl phosphonate followed by the catalytic reduction afforded dimethyl α-methylbenzylphosphonate in 74% yield from compound **7**. The reaction of 1-methylsulfinyl-1-methylthio-4-phenyl-1-butene with dimethyl phosphonate gave dimethyl (2-methylthio-1-phenethylvinyl)phosphonate in 21% yield.

Dialkyl phosphonates rapidly add to strongly activated C=C double bonds in the presence of basic catalysts, and the initial adducts are generally protonated to give phosphonates.[1] In previous papers, the reaction of phosphorus compounds with the 5,6-unsaturated 6-nitro-*xylo*-hexofuranose derivatives to give the 5-phosphino and 5-phosphinyl derivatives of D-glucose, that were *s*-alkylphosphorus derivatives, were reported.[2] The present paper deals with an alternative preparative method for *s*-alkylphosphonate.

Results and Discussion

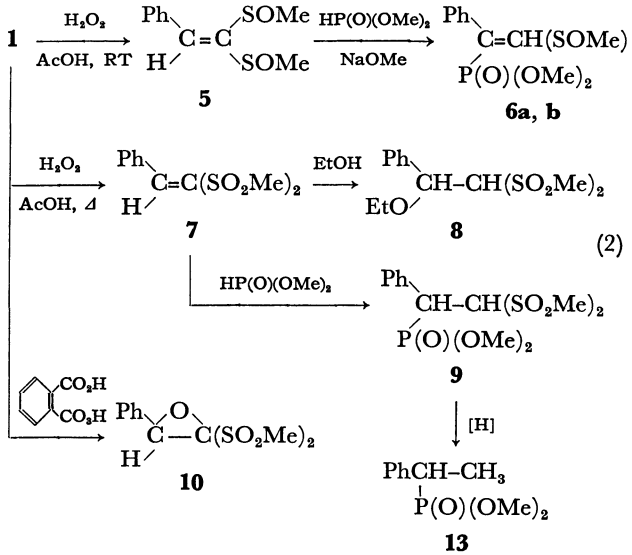
The reaction of (*E*)-β-methylsulfinyl-β-methylthiostyrene (**1**)[3] with dimethyl phosphonate in the presence of sodium methoxide under a nitrogen atmosphere at room temperature for a month afforded dimethyl (*Z*)-(2-methylthio-1-phenylvinyl)phosphonate (**3**) in 10% yield, but no corresponding initial adduct **2** was isolated. The photochemical reaction of compound **1** with dimethyl phosphonate or *O,O*-dimethyl thiophosphonate[4] afforded no such addition products as compound **2**, but gave the (*Z*)-isomer **4**,[3a] where the SMe signal in the NMR spectrum shifted from δ 2.25 to 2.45.



(1)

β,β-Bis(methylsulfinyl)styrene (**5**) has been prepared from compound **1** by the action of hydrogen peroxide in acetic acid.[5] The reaction of **5** with dimethyl phosphonate in the presence of sodium methoxide at room temperature for 2 weeks gave dimethyl (2-methylsulfinyl-1-phenylvinyl)phosphonate (**6**, 10% yield), which contained *E* and *Z* stereoisomers in the ratio of 1 : 1. The acid catalyzed reactions (*e.g.*, *p*-toluenesulfonic acid) of compounds **1** and **5** with dimethyl phosphonate were unsuccessful.

Oxidation of **1** with hydrogen peroxide in refluxing acetic acid afforded β,β-bis(methylsulfonyl)styrene (**7**) in 30% yield.[6] Compound **7** reacted with ethanol to give 1-ethoxy-2,2-bis(methylsulfonyl)-1-phenylethane (**8**) in excellent yield. The reaction of **7** with dimethyl phosphonate under a nitrogen atmosphere at 60 °C for 16 h gave the corresponding adduct **9** in 95% yield. It appears that the addition of phosphonate to ketene dimethyl dithioacetal derivatives is accelerated in the order –SMe<–SOMe≪–SO_2Me bearing in mind the reaction conditions.



(2)

The oxidation of **1** with hydrogen peroxide in acetic anhydride–acetic acid (1 : 1 v/v), or monoperoxyphthalic acid in ether gave the epoxide **10** in moderate yields. The reaction of 1-methylsulfinyl-1-methylthio-4-phenyl-1-butene (**11**)[7] with dimethyl phosphonate at 120 °C for 30 h afforded dimethyl (2-methylthio-1-phenethylvinyl)phosphonate (**12**) in 21% yield. The catalytic reduction of **3**, **6**, and **9** with Raney nickel gave dimethyl

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α-methylbenzylphosphonate (**13**) in 70—90% yields.

The Michaelis-Arbuzov and Michaelis-Becker reactions are important processes to prepare compounds having phosphorus-carbon bonds.[8] However, in some instances the reactions have been unsuccessful *e.g.*, the reaction of 3-*O*-benzyl-5-bromo-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose with sodium methylphosphide gave only olefinic products.[9] The addition reactions of phosphonates to ketones or hydrazones followed by 1 or 2 steps afforded *s*-alkylphosphonates in moderate yields.[10] The reaction described in this paper is an alternative method for the preparation of *s*-alkylphosphonates from esters as well as aldehydes.

The reaction of **1** and **5** with dimethyl phosphonate to give compounds **3** and **6** may be written as Eq. 1, *i.e.*, the initially formed adduct spontaneously loses methanesulfenic acid.[11] Compound **7** gave the corresponding adduct **9** attributed to the slow departure of methanesulfinic acid in this reaction condition.

Experimental

Material. Methyl methylthiomethyl sulfoxide was supplied by Nippon Soda Company, Ltd.

Measurements. Melting and boiling points were uncorrected. The ^{1}H-NMR spectra were run on Hitachi-Perkin-Elmer R-20 (60 MHz) and Hitachi R-24 (60 MHz) spectrometers with tetramethylsilane as an internal standard. The IR spectra were measured by Hitachi-Perkin-Elmer 337 and Japan Optics Laboratory A-3 infrared spectrophotometers.

*Reaction of (E)-β-Methylsulfinyl-β-methylthiostyrene (**1**) with Dimethyl Phosphonate.* Compound **1**[3] (1.5 g) was added to the mixture of dimethyl phosphonate (2 g) and sodium methoxide (1 g). After the introduction of nitrogen gas, the mixture was allowed to stand for 1 month at room temperature. Neutralization of the reaction mixture followed by extraction of the chloroform solution with saturated sodium chloride solution and evaporation of the volatile materials *in vacuo* afforded a syrup (R_f value 0.2, silica gel, eluent; benzene: ethyl acetate=1: 1 v/v). Purification of the syrup by column chromatography afforded 0.2 g of dimethyl (*Z*)-(2-methylthio-1-phenylvinyl)phosphonate (**3**, 10% yield). IR (neat) 1250 cm^{-1} (P=O); NMR ($CDCl_3$) δ 2.43 (s, 3H, SMe), 3.73 (d, J_{POCH}=12.0 Hz, 6H, POMe), 7.24 (d, J_{PCCH}=44.3 Hz, 1H, CH), and 7.34 (5H, Ph).

*Synthesis of β,β-Bis(methylsulfinyl)styrene (**5**).*[5] Treatment of **1** (5 g) with 35% aqueous hydrogen peroxide (4 ml) in acetic acid (15 ml) at room temperature for 30 h afforded the oxidation product, which was extracted with chloroform. Evaporation of the solvent followed by recrystallization from ethanol afforded 2.7 g of compound **5** (*meso* form, 51% yield), mp 113—115 °C (lit,[5] mp 112—113 °C).

*Synthesis of β,β-Bis(methylsulfonyl)styrene (**7**).*[6] Treatment of **1** (1.3 g) with 35% aqueous hydrogen peroxide (2.5 ml) in refluxing acetic acid (5 ml) for 6 h followed by neutralization of the reaction mixture, extraction of the chloroform solution with water, and evaporation of the solvent *in vacuo* afforded 1.3 g of a crude product (87% yield). Recrystallization from benzene–hexane gave 0.47 g of the pure compound **7** (30% yield), mp 136—137 °C. IR (KBr) 1330 and 1160 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 3.20 and 3.30 (s, 6H, SO_2Me), 7.6 (5H, Ph), and 8.48 (s, 1H, CH).

Found: C, 45.83; H, 4.66%. Calcd for $C_{10}H_{12}O_4S_2$: C, 46.15; H, 4.65%.

*Synthesis of 1,1-Bis(methylsulfonyl)-2-phenyloxirane (**10**).* Treatment of **1** (6 g) with 35% aqueous hydrogen peroxide (10 ml) in acetic anhydride (25 ml)–acetic acid (25 ml) for 5 days at room temperature followed by the same work-up as cited above afforded 3.5 g of **10** (42% yield), mp 158—160 °C. IR (KBr) 1330 and 1160 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 2.55 and 3.08 (s, 6H, SO_2Me), 4.98 (s, 1H, CH), and 7.38 (5H, Ph).

Found: C, 43.33; H, 4.54%. Calcd for $C_{10}H_{12}O_5S_2$: C, 43.48; H, 4.35%.

Oxidation of **1** (3 g) with monoperoxyphthalic acid (5.6 g) in ether at room temperature for 4 days afforded **10** (2.6 g) in 70% yield.

*Reaction of **5** with Dimethyl Phosphonate.* The mixture of dimethyl phosphonate (4.7 g), sodium methoxide (0.6 g), and **5** (1.5 g) in tetrahydrofuran (8 ml) under a nitrogen atmosphere was allowed to react for 2 weeks at room temperature. After the work-up as described for **1** with dimethyl phosphonate, the *E* and *Z* isomers of dimethyl (2-methylsulfinyl-1-phenylvinyl)phosphonate (**6a** and **6b**, 0.14g) were obtained in 10% yield. NMR ($CDCl_3$) δ 2.30 and 2.58 (s, 3H, SOMe), 3.63 and 3.65 (d, J_{POCH}=12.0 Hz, 6H, POMe), and 6.70—7.68 (m, 6H, Ph and CH).

*Reaction of **7** with Dimethyl Phosphonate.* A mixture of **7** (0.5 g) with an excess of dimethyl phosphonate (2 g) was heated for 16 h at 60 °C under a nitrogen atmosphere in a sealed tube. The removal of excess phosphonate *in vacuo* afforded dimethyl 2,2-bis(methylsulfonyl)-1-phenylethylphosphonate (**9**, *dl*-form, 0.67 g) in 95% yield, mp 154—157 °C. NMR ($CDCl_3$) δ 3.13 and 3.48 (s, 6H, SO_2Me), 4.15 and 4.35 (d, J_{POCH}=12.0 Hz, 6H, POMe), 4.50—6.00 (m, 2H, CH–CH), and 7.75—8.75 (m, 5H, Ph).

Found: C, 38.86; H, 5.17%. Calcd for $C_{12}H_{19}O_7PS_2$: C, 38.92; H, 5.14%.

*Reaction of **7** with Ethanol.* Reaction of **7** (1.3 g) with a large excess of hot ethanol (10 ml) afforded 1.36 g of adduct **8** (87% yield) in 72% yield from compound **1**, mp 145—149 °C. NMR ($CDCl_3$) δ 1.34 (t, J_{HH}=7.5 Hz, 3H, C–Me), 3.40 (s, 6H, SO_2Me), 3.83 (q, J_{HH}=7.5 Hz, 2H, O–CH_2), 4.45 and 5.84 (m, 2H, CH–CH), and 7.65 (m, 5H, Ph).

Found: C, 46.92; H, 5.96%. Calcd for $C_{12}H_{18}O_5S_2$: C, 47.04; H, 5.92%.

*Reaction of **11** with Dimethyl Phosphonate.* The reaction of **11**[7] (0.4 g) with dimethyl phosphonate (2.0 g) proceeded at 120 °C for 30 h. Evaporation of excess dimethyl phosphonate *in vacuo* afforded a syrup, which on separation by preparative TLC (silica gel, eluent: ethyl acetate) afforded phosphonate **12** in 21% yield. The reaction in the presence of *p*-toluenesulfonic acid gave a similar result. NMR (CCl_4) δ 2.12 (s, 3H, SMe), 2.00—2.90 (m, 4H, CH_2CH_2), 3.73 (d, J_{POCH}=12.0 Hz, 6H, POMe), and 7.05—7.50 (m, 6H, Ph and CH).

*Catalytic Hydrogenolysis of **9**.* Treatment of **9** (0.50 g) with hydrogen in the presence of Raney nickel (W-2) for 6 h in refluxing ethanol (20 ml) followed by filtration and evaporation afforded an oily material. The product in chloroform was washed with aqueous sodium hydrogencarbonate, and then dried over sodium sulfate. Evaporation of the solvent *in vacuo* gave dimethyl α-methylbenzylphosphonate (**13**) in 78% yield, bp 119—120 °C/1.5 mmHg (lit,[10b] bp 150—152 °C/2 mmHg). NMR (CCl_4) δ 1.40 (dd, J_{PCCH}=18.6 Hz and J_{HH}=7.5 Hz, 3H, C–Me), 3.00 (dq, J_{PCH}=23.0 Hz and J_{HH}=7.5 Hz, 1H, CH), 3.30 and 3.48 (d, J_{POCH}=10.3 Hz, 6H, POMe), and 7.16 (m, 5H, Ph).

Similar treatment of **3** and **6** afforded the same phosphonate in 70 and 90% yields, respectively.

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