Phosphonic Acids and Esters. X. Oxygen to Carbon Methyl Migration in the Reaction of Trimethyl Phosphite with Dimethyl Acetylenedicarboxylate[1,2]

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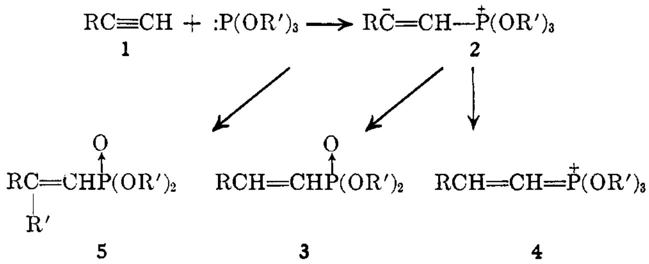
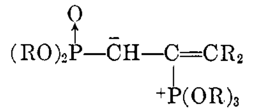
The thermal reactions of trialkyl phosphites with nonactivated acetylenes (**1**, R = aryl and alkyl and nonterminal analogs) have been shown to proceed through the formation of a dipolar intermediate **2** which collapses by an internal *cis*-β-elimination (R′ = C_2H_5, n-C_4H_9) to yield olefin and vinylphosphonate **3**.[2] Alternatively, **2** (R′ = CH_3) may be converted to **3** by an intermolecular process, *i.e.*, protonation by **1** to form a quasi-phosphonium salt **4** followed by nucleophilic dealkylation. In these reactions, the initial product **3** commonly undergoes β-attack by a second molecule of phosphite leading to the formation of alkylene-1,2-bisphosphonates.[2] An alternate mode of collapse of **2** involving oxygen to carbon alkyl migration to produce **5** was not observed in any of the cases studied because of the predominance of β-elimination and protonation processes. An alkyl migration of this type has been reported by Pudovik for dipolar intermediates **6** derived from the reaction of trialkyl phosphites with allenylphosphonates.[3] A related oxygen to oxygen alkyl migration has been observed in dipolar intermediates formed from trialkyl phosphites and α,β-acetylenic[4] and olefinic[5] acids. Thus the reaction of propiolic acid and trimethyl phosphite is reported to give **7**.





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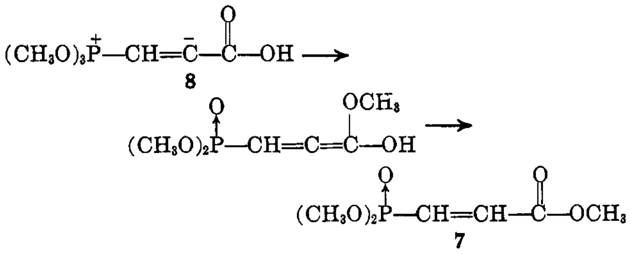
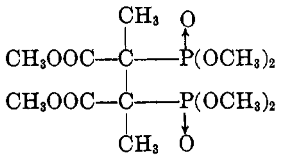
$$(RO)_2\overset{O}{\overset{\uparrow}{P}}-\bar{C}H-\underset{{}^{+}P(OR)_3}{\underset{|}{C}}=CR_2$$

These observations suggested that internal alkyl migrations only occur if the negative charge in the dipolar intermediate (**6**, **8**) is stabilized by either resonance or inductive interactions; in the absence of such stabilization (**2**), proton-transfer processes prevail.



$$\underset{\mathbf{8}}{(CH_3O)_3\overset{+}{P}-CH=\bar{C}-\overset{O}{\overset{\|}{C}}-OH} \longrightarrow (CH_3O)_2\overset{O}{\overset{\uparrow}{P}}-CH=C=\overset{OCH_3}{\overset{|}{C}}-OH \longrightarrow \underset{\mathbf{7}}{(CH_3O)_2\overset{O}{\overset{\uparrow}{P}}-CH=CH-\overset{O}{\overset{\|}{C}}-OCH_3}$$

In order to test this postulation, the reaction of trimethyl phosphite with dimethyl acetylenedicarboxylate has been examined. In this system, the *cis*-β-elimination process is minimized and no proton donor is present; consequently, the alkyl migration process (**2** → **5**) is the only reasonable reaction pathway. These reagents reacted quite exothermically in the absence of solvent; satisfactory reaction was only obtained in ether. Distillation of the reaction mixture gave 38% of 2,3-bis(carbomethoxy)-2,3-bis(dimethylphosphono)butane (**9**). The structure of **9** was established unequivocally on the basis of elemental analysis, molecular weight, infrared, and proton magnetic resonance (p.m.r.) spectra determinations. The p.m.r. spectrum of **9** showed P—O—CH_3 doublets at τ = 6.26 and 6.31 p.p.m. (J_{PH} = 10.8 c.p.s.), a $COOCH_3$ singlet at τ = 6.25 p.p.m., and a P—C—CH_3 doublet at τ = 7.96 p.p.m. (J_{PH} = 15.0 c.p.s.); the ratio of O-methyl to C-methyl was 3.0:1.0. The integrated intensities and peak multiplicities clearly eliminate any alternative structures (**10**, **11**) which would arise from protonation of dipolar intermediates.[6]



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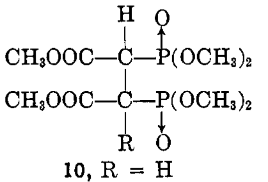
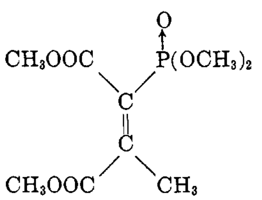


10, R = H
11, R = CH_3

It is most probable that the bisphosphonate **9** arises from the attack of trimethyl phosphite on the initially formed vinylphosphonate **12**. In the isolation of **9**, a lower boiling fraction was obtained which showed



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[1] This study was supported by the Petroleum Research Fund of the American Chemical Society.

[2] Part IX: C. E. Griffin and T. D. Mitchell, *J. Org. Chem.*, **30**, 1935 (1965).

[3] A. N. Pudovik, *Zh. Obshch. Khim.*, **20**, 92 (1950).

[4] K. M. Kirillova, V. A. Kukhtin, and T. M. Sudakova, *Proc. Acad. Sci. USSR, Chem. Sect.*, **149**, 209 (1963).

[5] G. Kamai and V. A. Kukhtin, *Zh. Obshch. Khim.*, **27**, 2372, 2376 (1957).

[6] Although no formal proton donor is present in the system, protonation of dipolar intermediates to form structures such as **10** and **11** was considered a possibility. In the corresponding dipolar intermediate formed by the reaction of benzyne and trimethyl phosphite, protonation is observed. No proton donor is present in this system, but apparently the phosphite functions as such. The mechanism of this reaction (V. A. Notaro, Ph.D. Thesis, University of Pittsburgh, 1965) has not been elucidated.

olefinic absorption at 1613 cm.$^{-1}$ and gave a positive qualitative test for unsaturation. The p.m.r. spectrum of this fraction indicated it to be a mixture containing *ca.* 90% of **12**, the presumed precursor of **9**, and *ca.* 10% of a trisubstituted olefin. The identity of these products could not be confirmed since the components of the mixture could not be separated.

The high reactivity observed in this reaction is consistent with the nucleophilic nature of the attack of trialkyl phosphites on acetylenes. The corresponding reaction with the less electrophilic acetylene, phenylacetylene, requires a reaction temperature of 120° for a period of 4 to 6 days. By contrast, the reaction leading to the formation of **9** requires a reaction period of 2 to 3 hr. at 35°.

An attempted study of the reaction of triethyl phosphite with both dimethyl acetylenedicarboxylate and ethyl propiolate led to inconclusive results. The reactions were extremely exothermic and led to the formation of inseparable mixtures and large amounts of nondistillable tars. The p.m.r. spectra of distillable fractions indicated the extensive formation of C-ethyl groups.

This study confirms the initial postulate regarding the reactivity of quasi-phosphonium dipoles (**2**). In the absence of extensive anionic stabilization by electron-attracting groups (**2**, R = aryl, alkyl), protonative decomposition occurs, while oxygen to carbon alkyl transfers predominate in more highly stabilized anions [**2**, R = COOR′, P(O)(OR′)$_2$].

Experimental[7]

Reaction of Trimethyl Phosphite with Dimethyl Acetylenedicarboxylate.—Dimethyl acetylenedicarboxylate (14.2 g., 0.100 mole) was added dropwise at 5–10° to a solution of 25.3 g. (0.204 mole) of trimethyl phosphite in 200 ml. of anhydrous ether. After addition was completed, the reaction mixture was stirred for 1 hr. at room temperature and then refluxed for 1 hr.; all of these operations were carried out under an atmosphere of nitrogen. Upon cooling, a thick oil separated from the reaction mixture; the ethereal layer was reduced in volume to afford additional quantities of the oil. The combined oils were distilled under reduced pressure to give dimethyl acetylenedicarboxylate (8.7% recovery) and 14.7 g. (37.7%) of **2,3-bis(carbomethoxy)-2,3-bis(dimethylphosphono)butane** (**9**), b.p. 190° (0.50 mm.). This material crystallized on standing for a few days at room temperature; recrystallization from carbon tetrachloride gave material of m.p. 164.5–165.5°.

Anal. Calcd. for $C_{12}H_{24}O_{10}P_2$: C, 36.93; H, 6.19; P, 15.88; mol. wt., 390. Found: C, 37.15, 37.19; H, 5.93, 6.02; P, 16.05, 16.03; mol. wt., 368, 377.[8]

The infrared spectrum of **9** (in $CHCl_3$) showed bands at 2985 s, 2950 s, 2899 w, 2841 s, 1718 s, 1449 s, 1429 s, 1385 s, 1227 s, 1087 m, 1036 s, 980 m, and 960 m cm.$^{-1}$.

A lower boiling fraction, b.p. 126–126.5° (0.50 mm.), was also obtained during the isolation of **9**. The infrared spectrum of this material (film) showed absorptions at 1721 s (ester C=O), 1613 w (C=C), 1252 s (P—O), 1179 m (P—O—CH_3), 1024 s [P—O—C-(alkyl)], and 830 m cm.$^{-1}$ (C—H out-of-plane deformation, trisubstituted olefins). The p.m.r. spectrum showed C-methyl signals at τ = 7.7–8.0 p.p.m., an O-methyl complex centered at τ = 6.3 p.p.m., and vinyl absorptions at τ = 3.1–4.0 p.p.m. Attempted purification of this fraction by distillation and silicic acid chromatography was unsuccessful.

Benzylation and Benzoylation of Methyl Phenacyl Sulfone

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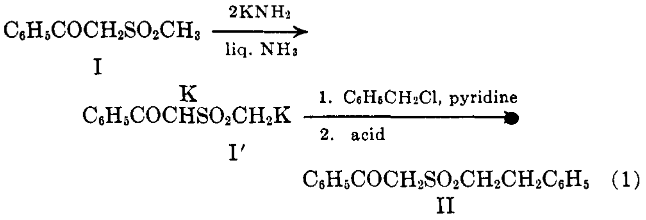
Benzylation at the terminal methyl group of benzenesulfonylacetone by means of its dipotassio salt has previously[1] been described. We now report the benzylation at the terminal methyl group of keto sulfone I by means of its dipotassio salt (I′) in pyridine (eq. 1).



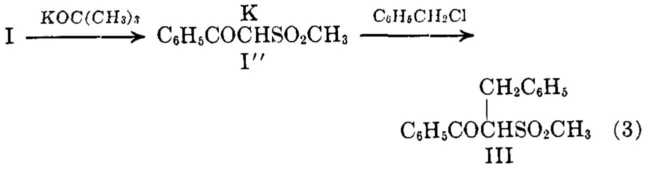
$$\underset{\text{I}}{C_6H_5COCH_2SO_2CH_3} \xrightarrow[\text{liq. NH}_3]{2KNH_2} \underset{\text{I}'}{C_6H_5CO\overset{K}{C}HSO_2CH_2K} \xrightarrow[\text{2. acid}]{\text{1. }C_6H_5CH_2Cl\text{, pyridine}} \underset{\text{II}}{C_6H_5COCH_2SO_2CH_2CH_2C_6H_5} \quad (1)$$

The structure of the alkylation product was established by independent synthesis of II from phenacyl bromide and sodium 2-phenylethylsulfinate (eq. 2).

$$C_6H_5COCH_2Br + C_6H_5CH_2CH_2SO_2Na \longrightarrow \text{II} \qquad (2)$$

When the benzylation reaction was attempted in liquid ammonia, a high yield of stilbene and no benzoyl product was obtained. This may indicate that an appreciable amount of potassium amide was present in equilibrium with I′, since benzyl chloride is known to be converted to stilbene by the amide ion.[2]

Benzylation of the monopotassio salt (I″) of I, prepared by means of potassium *t*-butoxide in *t*-butyl alcohol gave 1,3-diphenyl-2-methylsulfonylpropan-1-one (III) in 81% yield (eq. 3).



$$\text{I} \xrightarrow{KOC(CH_3)_3} \underset{\text{I}''}{C_6H_5CO\overset{K}{C}HSO_2CH_3} \xrightarrow{C_6H_5CH_2Cl} \underset{\text{III}}{C_6H_5CO\overset{CH_2C_6H_5}{\overset{|}{C}}HSO_2CH_3} \quad (3)$$

That the product was the expected C-benzyl derivative III and not the possible O-benzyl derivative was shown by its infrared spectrum which had a strong carbonyl peak at 1695 cm.$^{-1}$. It was shown not to be the only other possible C-benzyl derivative II by comparison of infrared spectra and by the mixture melting point method. When the reaction was carried out in dimethyl sulfoxide, the same product (III) was obtained in lower yield. It is interesting to note that carbon alkylation only was obtained in this solvent which favors oxygen alkylation in some other ambident anions.[3]

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[7] Infrared spectra were determined on a Beckman IR-8 spectrophotometer. P.m.r. spectra were determined with a Varian Associates A-60 spectrometer on 20–30% solutions in deuteriochloroform using tetramethylsilane as an internal standard. Microanalyses were performed by Galbraith Microanalytical Laboratories.

[8] Molecular weight determinations were carried out with a Mechrolab Model 301A vapor pressure osmometer using dilute solutions in benzene at 37°.

[1] W. I. O'Sullivan, D. F. Tavares, and C. R. Hauser, *J. Am. Chem. Soc.*, **83**, 3453 (1961).

[2] C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Brodhag, *ibid.*, **78**, 1653 (1956).

[3] See N. Kornblum, R. Seltzer, and P. Haberfield, *ibid.*, **85**, 1148 (1963).