Nucleophilic Displacements α to Sulfonyl Groupings

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Thiophenoxide ion in dimethylformamide solution displaces the halogen atom in halomethyl and α-halobenzyl phenyl sulfones to give high yields of the corresponding phenylthiomethyl and α-phenylthiobenzyl phenyl sulfones. A study of the effect of the nature of the halogen (bromine or chlorine) and the effect of protic solvents on the proportion of displacement *vs.* reduction products was made. Thiophenoxide ion in either dimethylformamide or 33% methanol–67% dimethylformamide solvents reacted with halomethyl phenyl sulfones to give a nearly quantitative yield of phenylthiomethyl phenyl sulfone (**2**). In ethanol solution, thiophenoxide ion reacted with the halomethyl phenyl sulfones to give *ca.* 80% **2** and 20% methyl phenyl sulfone (**3**). In the reaction of thiophenoxide ion with α-halobenzyl phenyl sulfones, α-phenylthiobenzyl phenyl sulfone was obtained in anhydrous dimethylformamide, while this same reaction in the presence of small amounts of protic solvent gave large amounts of benzyl phenyl sulfone (**7**). It is concluded that the halomethyl phenyl sulfones are undergoing SN2 reactions but that the α-halobenzyl phenyl sulfones are probably reacting by a reduction–displacement sequence.

The reaction of bromomethyl *p*-tolyl sulfone with sodium *n*-butyl mercaptide in ethanol has been reported to give 76% of methyl *p*-tolyl sulfone.[1] Displacement on carbon also apparently failed in a similar reaction with sodium *p*-tolyl mercaptide, judging from the isolation of *p*-tolyl disulfide as the major reaction product.[1] These observations and studies of the behavior of compounds like $C_6H_5SO_2CH_2Cl$ and $ClCH_2SO_3Na$ with nucleophiles has led to the conclusion that arylsulfonyl and sulfonate groupings exert a strong retarding effect on SN2 displacements at the α-carbon atom.[2] This effect does not extend to the β or to more distant positions.[3] The retarding effect has been attributed to a steric blocking of the approach of the nucleophile to the α-carbon atom by the sulfonyl oxygen atoms, the radius of which is considerably extended by their residual negative charges.[2,3] In terms of Ingold's classification of structural kinetic effects operating on SN2 reactions, this is a combination of a polar effect and a steric effect.[4] It may alternatively be described as a field effect.[5] In another study we observed what appeared to be a displacement reaction α to a sulfone grouping using dimethylformamide (DMF) solvent. The nucleophilicity of anions in dipolar aprotic solvents like DMF has been found to be greatly enhanced, presumably because of lessened solvation of the anions in this poorly hydrogen-bonding medium.[6] One would also expect a lesser degree of solvation around the sulfonyl oxygen atoms in such solvents. Both of these effects should operate to make SN2 displacements for α-halo sulfones much more facile in dipolar aprotic solvents than in protic solvents. A number of experiments to test this idea have been carried out.

Results

The reaction of potassium thiophenoxide with either bromomethyl phenyl sulfone (**1a**) or chloromethyl phenyl sulfone (**1b**) in dimethylformamide (DMF) gave high yields of phenylthiomethyl phenyl sulfone (**2**). The presence of water in a 10:1 mol ratio to **1** or of methanol in as much as a 100:1 mol ratio did not affect the result.

$$\underset{\mathbf{1},\ X = Br,\ Cl}{C_6H_5SO_2CH_2X} + C_6H_5SK \xrightarrow{DMF} \underset{\mathbf{2}}{C_6H_5SO_2CH_2SC_6H_5} + K^+X^-$$

A slow displacement of the bromine atom in **1a** was also effected by reaction with lithium chloride in DMF (10% conversion in 4 hr at 80°). On the other hand, no reaction occurred under these conditions with sodium cyanide in DMF. After 10 hr at 70–80° with piperidine in DMF 80% of **1a** was recovered and a small amount of methyl phenyl sulfone (**3**) was obtained.

Contrary to the earlier report,[1] the SN2 displacement product (**2**) was the major product from **1a** and sodium thiophenoxide, even in ethanol solution, although about 20% reduction product, methyl phenyl sulfone (**3**), was also obtained. A similar result was obtained in methanol. The products isolated from this latter reaction were **2** (80%), **3** (9%), and phenyl orthothioformate (**4**, 2%).

$$\underset{\mathbf{1a}}{C_6H_5SO_2CH_2Br} \xrightarrow[CH_3OH,\ 12\text{-hr reflux}]{C_6H_5SNa} \underset{\mathbf{2}\ (80\%)}{C_6H_5SO_2CH_2SC_6H_5} + \underset{\mathbf{3}\ (9\%)}{C_6H_5SO_2CH_3} + \underset{\mathbf{4}\ (2\%)}{(C_6H_5S)_3CH}$$

A larger amount of **4** (31%) was obtained in ethanol solvent, and the amount was observed to increase with time. Its source was traced to a slow reaction between **2** and phenyl disulfide; the latter was formed as a consequence of the production of the reduction product (**3**). A 78% yield of **4** was obtained in a separate experiment using **2** and phenyl disulfide in ethanol containing sodium ethoxide.

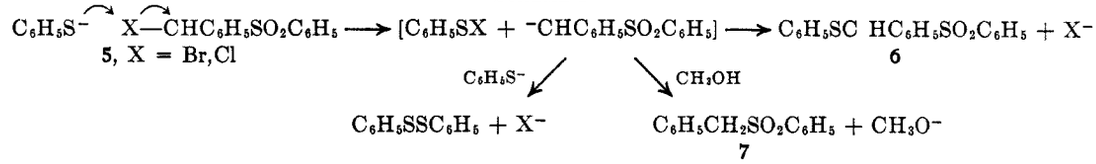
$$NaOC_2H_5 + \underset{\mathbf{2}}{C_6H_5SO_2CH_2SC_6H_5} + C_6H_5SSC_6H_5 \xrightarrow[(C_2H_5O^-)]{C_2H_5OH} \underset{\mathbf{4}\ (78\%)}{(C_6H_5S)_3CH} + C_6H_5SO_2Na + C_2H_5OH$$

The reaction of **1a** with sodium ethoxide in ethanol gave **3** as the major product. This is in agreement with the results of Ziegler and Conner.[1]

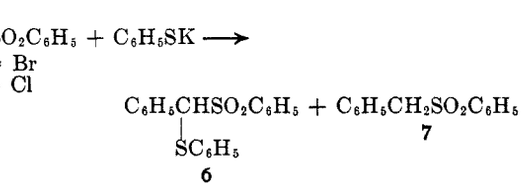
Reaction of α-bromo- or α-chlorobenzyl phenyl sulfone (**5a** and **5b**, respectively) with potassium thiophenoxide in DMF gave *ca.* 95% α-phenylthio-

(1) W. M. Ziegler and R. Conner, *J. Amer. Chem. Soc.*, **62**, 2596 (1940).
(2) F. G. Bordwell and G. D. Cooper, *ibid.*, **73**, 5184 (1951), and references cited therein.
(3) F. G. Bordwell and W. T. Brannen, Jr., *ibid.*, **86**, 4645 (1964).
(4) C. K. Ingold, *Quart. Rev.* (London), **11**, 1 (1959).
(5) C. Y. Meyers, *Tetrahedron Lett.*, No. 24, 1125 (1962).
(6) See A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).

SCHEME I



benzyl phenyl sulfone (**6**) and 5% reduction product, benzyl phenyl sulfone (**7**). In the presence of a 7.5:1 mol ratio of methanol to **5**, the ratio of **6** to **7** was 65:35 from **5a** and 80:20 from **5b**. When 50% methanol–DMF by volume was used as the solvent, only **7** was obtained from either **5a** or **5b**.



Reaction of **5a** with excess refluxing piperidine gave **7** as the only isolable product (93%).

Discussion

The most likely mechanism for the reactions of **1a** and **1b** with thiophenoxide ion to give **2** in alcohol or DMF solvents is SN2 displacement by thiophenoxide ion on carbon. The only alternative mechanism that needs to be considered is attack of thiophenoxide ion on halogen to produce an α-sulfonyl carbanion and a benzenesulfenyl halide (C_6H_5SX). If these species were to react with one another faster than with solvent or thiophenoxide ion, this could serve as an alternative route to **2**. However, the reaction of the carbanion $C_6H_5SO_2CH_2^-$ with alcohol solvents is extremely fast.[7] Furthermore, the displacement of Br from **1a** by Cl^- seems unlikely to involve attack of the nucleophile on halogen. These data argue against the carbanion mechanism but cannot rule it out completely. It is interesting to note in this connection that in ethanol solution ethoxide ion attacks **1a** exclusively at the bromine atom, whereas thiophenoxide ion attacks **1a** primarily at the carbon atom (assuming the SN2 mechanism). This is just the reverse of what would have been predicted on the basis of the concept of "hard and soft acids and bases."[10] Of course, if **2** is assumed to be formed by attack of thiophenoxide ion on halogen, there would be no conflict with the theory.

The $C_6H_5SO_2CHXC_6H_5$ system (**5**) should be much more prone to nucleophilic attack on halogen than the $C_6H_5SO_2CH_2X$ system (**1**). The $(C_6H_5SO_2CHC_6H_5)^-$ carbanion is much more stable (a better leaving group) than the $C_6H_5SO_2CH_2^-$ carbanion, judging from the fact that the pK_a of $C_6H_5CH_2SO_2CH_2C_6H_5$ is about 5 units lower than that of $C_6H_5SO_2CH_3$,[8] and is, therefore, presumably much more readily produced by nucleophilic attack on halogen. Also, the change from **1** to **5** may retard nucleophilic attack on carbon, judging from the slower rate for displacement of Cl^- by I^- from $C_6H_5CHClCOCH_3$ compared with $ClCH_2COCH_3$.[11] The data show that **5** is indeed much more susceptible to reduction than is **1**. Note, for example, that reduction of **5** by thiophenoxide ion is complete in methanol or ethanol, whereas with **1** only 10–20% reduction occurs. It seems likely, then, that attack of $C_6H_5S^-$ occurs on halogen for **5** in DMF, and that the C_6H_5SX which is produced reacts with the carbanion before the two species diffuse apart. In the presence of methanol (7:5:1 molar ratio to 1) this mechanism requires that C_6H_5SX win out over CH_3OH in competition for the carbanion, since **6** is formed in preference to **7** under these conditions (Scheme I).

There is analogy for this pathway in the reaction in aprotic solvents of triphenylphosphine with α-halo ketones[12,13] and α-halo sulfones[14] to give displacement at halogen followed by rearrangement to the normal SN2 product. Complete reduction occurs in these reactions in the presence of 2 equiv of methanol; α-bromo ketones are far more reactive than α-chloro ketones.[15]

With **5a** or **5b** only partial reduction occurs even with a 7.5:1 ratio of methanol to halide. This requires that C_6H_5SX be far more reactive toward the sulfonyl carbanion than is $(C_6H_5)_3PX$ toward the enolate ion or the sulfonyl carbanion, if comparable mechanisms are to operate.

Displacement at the halogen atom would be expected to be more sensitive to the nature of the halogen than would displacement at carbon.[10] Therefore, **5a** would be expected to be much more reactive than **5b**, if attack is on halogen. This prediction was borne out. A qualitative comparison of the rates of reaction of **5a** and **5b** with thiophenoxide ion in anhydrous and methanolic DMF showed that **5a** reacted >600 times as fast as **5b** under the same conditions. This large difference in rates is more compatible with displacement at the halogen atom than with displacement at the carbon center. The leaving-group effect going from chlorine to bromine in normal SN2 displacements is *ca.* 50.[16] These data support the carbanion mechanism for the production of **6**, at least from **5a**. Also, if **6** were being produced from the chloride **5b** solely by displacement at carbon and **7** by displacement at halogen, one might have expected the increase in reduction product in going from the

(7) Using the pK_a value of 27 determined for $C_6H_5SO_2CH_3$ in DMSO,[8] the calculated rate for the combination of $C_6H_5SO_2CH_2^-$ with a proton from methanol would be $k_{-1} = k_1K_{CH_3OH}/K_{C_6H_5SO_2CH_3} \cong 2 \times 10^8\ M^{-1}\ sec^{-1}$.[9]

(8) F. G. Bordwell, R. H. Imes, and E. C. Steiner, *J. Amer. Chem. Soc.*, **89**, 3905 (1967).

(9) The rate of exchange for $C_6H_5SO_2CH_3$ in CH_3OD catalyzed by methoxide ion is $2.1 \times 10^{-3}\ M^{-1}\ sec^{-1}$ at 25° (D. A. Schexnayder, unpublished results). The pK_a for $C_6H_5SO_2CH_3$ in methanol is probably not 27, but the order of magnitude is no doubt correct.

(10) R. G. Pearson and J. Songstad, *ibid.*, **89**, 1827 (1967).

(11) A. W. Fort, *ibid.*, **84**, 2620 (1962), footnote 17.

(12) I. J. Borowitz and R. Virkhaus, *ibid.*, **85**, 2183 (1963); see, however, I. J. Borowitz and H. Parnes, *J. Org. Chem.*, **32**, 3560 (1967).

(13) P. A. Chopaud, R. F. Hudson, and G. Klopman, *J. Chem. Soc.*, 1379 (1965).

(14) H. Hoffman and H. Förster, *Tetrahedron Letters*, 1547 (1963).

(15) I. J. Borowitz and L. I. Grossman, *ibid.*, 471 (1962).

(16) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw Hill Book Co., Inc., New York, N. Y., 1962, p 30.

chloride (**5b**) to the bromide (**5a**) to be much larger than that observed.

The reaction of **2** with phenyl disulfide to give **4** must occur by way of bis(phenylthio)methyl phenyl sulfone (**8**). Displacements initiated by nucleophiles, like the carbanion derived from **2**, on the sulfur atom of disulfides are common.[17,18] The formation of **4** from **8** can be pictured as a direct displacement (S$_N$2) or as a solvolysis in which the carbonium ion is captured by thiophenoxide ion. The latter path seems more likely.[19]

$$C_6H_5SO_2CH_2SC_6H_5 \xrightarrow[C_2H_5OH]{C_2H_5O^-} [C_6H_5SO_2CHSC_6H_5]^- \xrightarrow{C_6H_5SSC_6H_5}$$
2

$$[C_6H_5SO_2CH(SC_6H_5)_2] + C_6H_5S^-$$
8

$$\mathbf{8} \xrightarrow{C_2H_5OH} C_6H_5SO_2^- + [(C_6H_5S)_2CH^+] \xrightarrow{C_6H_5S^-} (C_6H_5S)_3CH$$
4

Experimental Section

Analyses were performed by H. Beck, Northwestern University, Evanston, Ill. 60201.

Reaction of Bromomethyl Phenyl Sulfone (1a) with Potassium Thiophenoxide in DMF.—To a solution of 5.00 g (21.3 mmol) of **1a**[20] in 30 ml of dry DMF was added 5.00 g of potassium thiophenoxide. The mixture turned bright yellow, and a precipitate began to form after a few minutes. This mixture was stirred under an atmosphere of nitrogen for 12 hr at room temperature and then poured into water and extracted with ether. From the ether extract was obtained an oil which was crystallized from carbon tetrachloride–hexane to give 4.7 g of phenylthiomethyl phenyl sulfone (**2**), mp 60.5–62.0°. Chromatography of the mother liquor over 60 g of silica gel gave an additional 500 mg (off with 5% ether in hexane) to bring the yield to 5.2 g (93%). The nmr spectrum (carbon tetrachloride) showed aromatic protons (10 H) and a singlet at τ 5.78 (2 H). Breslow and Mohacsi[21] list this peak at τ 5.74 and mp 55–57°.

Anal. Calcd for $C_{13}H_{12}O_2S_2$: C, 59.06; H, 4.58. Found: C, 59.09; H, 4.66.

This same reaction repeated with 2% water (by volume) in DMF gave essentially the same result.

Oxidation of 200 mg of phenylthiomethyl phenyl sulfone with 3 ml of 30% hydrogen peroxide in 10 ml of acetic acid at *ca.* 100° for 3 hr followed by the usual work-up gave 150 mg of bis(phenylsulfonyl)methane, mp 122.5–123° from ethanol (lit.[22] mp 120–121°).

Reaction of 1a with Sodium Thiophenoxide in Alcohol Solvents.—To a solution of 500 mg (4.54 mmol) of benzenethiol in 15 ml of absolute methanol in which 200 mg of sodium metal had been dissolved was added 500 mg (2.13 mmol) of **1a**. This mixture stood at reflux for 12 hr and was worked up by pouring it into water and extracting it with ether. An nmr spectrum of the crude reaction mixture showed there to be present 90% **2** and 10% methyl phenyl sulfone (**3**) along with a small amount of phenyl orthothioformate (**4**). These products could be isolated by column chromatography over silica gel: **4** (15 mg (2%), crystallized from pentane; mp 39–39.5° undepressed on admixture with an authentic sample[23]) was eluted with 15% benzene in hexane; **2** (450 mg, 80%) was eluted with 5% ether in hexane; **3** (30 mg, 9%) was eluted with 10% ether in hexane.

This same reaction in absolute ethanol gave (by nmr analysis) 49% **2**, 20% **3**, and 31% **4**.

Reaction of 1a with Potassium Thiophenoxide in 33% Methanol–DMF.—To a solution of 750 mg (5.2 mmol) of potassium thiophenoxide in 5 ml of methanol (124 mmol) and 10 ml of DMF was added 300 mg (1.28 mmol) of **1a**. This mixture was held at reflux for 8 hr and then worked up as usual. An nmr spectrum of the crude reaction mixture showed no **3** present. Crystallization from ether–hexane gave 310 mg (92%) of **2**, mp 61–63°. This same reaction with **1b**[3] (300 mg) gave the same result.

Reaction of 1a with Sodium Ethoxide in Ethanol.—To a solution of 400 mg of sodium metal dissolved in 20 ml of absolute ethanol was added 300 mg (1.28 mmol) of **1a**. This mixture was held at reflux for 12 hr, and the resulting dark brown mixture was worked up as usual. An nmr spectrum of the crude reaction mixture showed **3** to be the only compound present containing aromatic protons. The oil was then taken up in methanol, treated with charcoal, and cooled, and the resulting precipitate was collected to give 130 mg (65%) of **3**, mp 85–86° (lit.[24] mp 88°).

Attempted Reaction of the Bromo Sulfone 1a with Sodium Cyanide.—Treatment of **1a** with 1 *M* sodium cyanide in DMF at 80–90° for 4 hr followed by the usual work-up gave only recovered starting material (over 50%). This same reaction in DMSO solvent at 80° gave extensive decomposition with a low recovery of starting material.

Reaction of Chloromethyl Phenyl Sulfone (1b)[1] with Potassium Thiophenoxide in DMF.—A solution of 2.0 g (10.6 mmol) of **1b** and 3.0 g (20 mmol) of potassium thiophenoxide in 20 ml of dry DMF under nitrogen was heated at 80° for 1 hr and then worked up in the usual manner. The thio ether was crystallized from ether–hexane to give 2.3 g (83%) of phenylthiomethyl phenyl sulfone, mp 60–62°.

Reaction of Bromomethyl Phenyl Sulfone (1a) with Lithium Chloride in DMF.—A solution of 2.0 g of **1a** and 2.5 g of anhydrous lithium chloride in 20 ml of dry DMF stood at 80° for 4 hr. The usual work-up gave an oil which was shown by nmr analysis to be 90% bromo sulfone **1a** and 10% chloro sulfone **1b**.

Reaction of 2 with Phenyl Disulfide in Basic Ethanol.—To a solution of 1.0 g of sodium metal dissolved in 20 ml of absolute ethanol was added 1.0 g (3.8 mmol) of **2** and 830 mg (4.0 mmol) of phenyl disulfide. This mixture was held at reflux for 5 hr and worked up as usual. An nmr spectrum showed no **2** left and the only proton visible outside the aromatic region was attributable to **4**. Chromatography over silica gel gave **4** as an oil which was eluted with 15% benzene in hexane. The oil was crystallized from pentane to give 1.0 g (78%) of **4**, mp 39–39.5°.

α-Bromobenzyl Phenyl Sulfone (5a).—To a solution of 11.0 g (40.5 mmol) of phenylsulfonylphenylacetic acid[25] dissolved in 100 ml of water containing 27.6 g (200 mmol) of potassium carbonate was added 8.0 g (50 mmol) of bromine dissolved in 50 ml of a 20% potassium bromide solution. The resulting mixture was stirred for 6 hr at room temperature and filtered. The solid was washed with water and a small amount of ethanol and recrystallized from ethanol–chloroform to give 6.5 g (50%) of **5a**, mp 193–194°.

Anal. Calcd for $C_{13}H_{11}BrO_2S$: C, 50.16; H, 3.56. Found: C, 50.18; H, 3.53.

Reaction of α-Bromobenzyl Phenyl Sulfone (5a) with Piperidine.—A solution of 500 mg (1.61 mmol) of **5a** in 10 ml of piperidine was held at reflux for 50 hr. The piperidine was removed *in vacuo* and an nmr spectrum of the resulting solid showed it to be benzyl phenyl sulfone (**7**). Crystallization from ethanol following a treatment with activated charcoal gave 350 mg (93%) of **7**, mp 147–148° (lit.[26] mp 149–150°).

Reaction of 5a with Potassium Thiophenoxide in DMF and Methanol–DMF.—To a solution of 500 mg of potassium thiophenoxide in 10 ml of dry DMF was added 300 mg (0.97 mmol) of **5a**. This mixture stood at room temperature for 1 hr and was then worked up as usual. An nmr spectrum of the resulting oil showed it to be *ca.* 95% α-phenylthiobenzyl phenyl sulfone (**6**) and *ca.* 5% benzyl phenyl sulfone (**7**). This material was passed over 25 g of silica gel and **6** was eluted with 15% ether in hexane to yield 320 mg (89%). This was recrystallized from hexane to a product of mp 92–93°. Further elution with 15% ether in hexane gave 10 mg (4%) of **7**.

(17) A. J. Parker, "Organic Sulfur Compounds," Vol. I, edited by N. Kharasch, Pergamon Press Inc., New York, N. Y., 1961, pp 103.
(18) G. Leandri and A. Tundo, *Ann. Chim.*, **44**, 518 (1954).
(19) Bis(phenylthio)chloromethane is highly reactive toward solvolysis; see H. Böhme and J. Roehr, *Ann.*, **648**, 21 (1961).
(20) F. G. Bordwell, J. M. Williams, Jr., and B. B. Jarvis, *J. Amer. Chem. Soc.*, in press.
(21) R. Breslow and E. Mohacsi, *ibid.*, **84**, 684 (1962).
(22) R. Otto and J. Tröger, *Ber.*, **25**, 3425 (1892).
(23) J. Hine, *J. Amer. Chem. Soc.*, **72**, 2438 (1950).
(24) H. Bohme and H. Fischer, *Ber.*, **75**, 1310 (1942).
(25) K. Fuchs, *Monatsh.*, **53/54**, 438 (1929).
(26) H. Böhme and D. Morf, *Chem. Ber.*, **90**, 446 (1957).

Anal. (for **8**). Calcd for $C_{19}H_{16}O_2S_2$: C, 61.27; H, 4.33. Found: C, 61.35; H, 4.31.

This same reaction repeated in 10 ml of DMF (10 ml) containing 0.5 ml (12 mmol) of methanol with 600 mg of potassium thiophenoxide and 500 mg (1.6 mmol) of **5a** at 70° for 30 min gave a 65:35 mixture of **6** and **7**, respectively, while in a 50:50 mixture of methanol–DMF (5 ml each), **5a** gave only **7** in near quantitative yield.

Reaction of α-Chlorobenzyl Phenyl Sulfone (5b) with Potassium Thiophenoxide in DMF and Methanol–DMF.—Reaction of **5b**[27] with potassium thiophenoxide in DMF and in 50% methanol–DMF was carried out in the same manner as that of **5a** and gave identical results. In 5% methanol–DMF the reaction was performed in the same manner as that of **5a** but gave instead 80% **6** and 20% **7** (nmr analysis).

Reaction of 1b with Sodium Ethoxide in Ethanol.—To a solution of 400 mg of sodium metal dissolved in 20 ml of absolute ethanol was added 500 mg (2.6 mmol) of **1b**. This mixture stood at reflux for 18 hr and was then worked up as usual. An nmr spectrum of the resulting oil showed about a 4:1 mixture of recovered **1b** and methyl phenyl sulfone (**3**). The spectrum was contaminated with several smaller peaks which were not readily identifiable.

Reaction of 1a with Piperidine in DMF.—A mixture of 300 mg (1.29 mmol) of **1a** and 200 mg (2.35 mmol) of piperidine were held at 70–80° for 10 hr in 15 ml of dry DMF. The mixture was poured into water and extracted with ether. An nmr spectrum of the crude reaction mixture showed **1a** and piperidine present. When the piperidine was removed by washing with dilute hydrochloric acid, a small amount of methyl phenyl sulfone (**3**) was visible in the nmr spectrum. Crystallization from ethanol of the crude reaction mixture after removal of the piperidine gave 240 mg (80%) of recovered **1a**.

Determination of the Relative Rates of Reaction of 5a and 5b with Thiophenoxide Ion.—Aliquots (5 ml) were taken of a solution of 625 mg (2.0 mmol) of **5a** in 20 ml of dry DMF to which 445 mg (3.0 mmol) of potassium thiophenoxide in 20 ml of dry DMF had been added. The first aliquot (1 min) showed no **5a** present (nmr analysis). This same procedure with **5b** (515 mg, 2.0 mmol) showed that the reaction was not complete for *ca.* 10 hr (therefore $k_{Br}/k_{Cl} > 600$).

The procedure for 50% methanol–50% DMF was as follows. To a solution of 315 mg (1.0 mmol) of **5a** in 10 ml of DMF and 7 ml of methanol was added 3 ml of a solution of 120 mg (5.2 mg-atoms) of sodium metal and 550 mg (5.0 mmol) of benzenethiol dissolved in 10 ml of methanol (1.5 mmol of sodium thiophenoxide added). The half-life of this reaction was *ca.* 1 hr. Under these same conditions, **5b** showed no sign of reaction (nmr analysis) after 27 hr.

Registry No.—**2**, 15296-86-3; **3**, 3112-85-4; **4**, 4832-52-4; **5a**, 15296-88-5; **7**, 3112-88-7; **8**, 15296-89-6.

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(27) R. Otto, *J. Prakt. Chem.*, **40**, 505 (1889).

α,β-Unsaturated Aldehydes as Acceptors in the Oxyphosphorane Carbon–Carbon Condensation. Hydrolyses of Five-Membered Cyclic Pentaoxyphosphoranes and Phosphate Esters[1]

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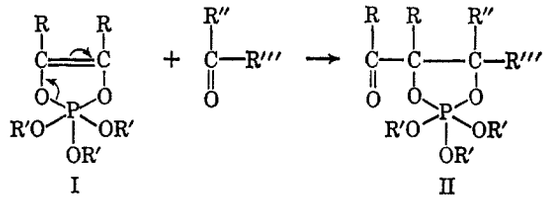
2,2,2-Trimethoxy-4,5-dimethyl-2,2,dihydro-1,3,2-dioxaphospholene performed a nucleophilic 1,2 addition to the carbonyl function and not a 1,4 addition to the olefinic carbon of acrolein. The product was 2,2,2-trimethoxy-4β-methyl-4α-acetyl-5α-vinyl-2,2-dihydro-1,3,2-dioxaphospholane; only the diastereomer with a *cis*-CH_3/H was obtained. Hydrolysis of the five-membered pentaoxyphosphorane gave the two diastereomers at phosphorus of the five-membered cyclic phospho triester. The cyclic phospho triesters underwent an extraordinarily rapid reaction with methanol and gave the corresponding open-chain phospho triester derived from a γ-unsaturated α,β-dihydroxy ketone. The kinetically controlled product had the phosphate at the α position, but the thermodynamically stable product had the phosphate at the β position. The open phospho triester regenerated the cyclic phospho triester upon distillation under vacuum. Hydrolysis of the five-membered pentaoxyphosphorane with an excess of water gave minor amounts of the open-chain β-phospho triester and major amounts of the open phospho monoester derived from the γ-unsaturated α,β-dihydroxy ketone. The kinetically controlled product had the dihydrogen phosphate group at the α carbon, while the thermodynamically stable product had the dihydrogen phosphate group at the β carbon. The five-membered cyclic phospho triester underwent a very rapid hydrolysis with 1 mol equiv of water and gave the five-membered cyclic phospho diester and the open-chain β-phospho triester.

The nucleophilic addition[3] of 2,2,2-trialkoxy-2,2-dihydro-1,3,2-dioxaphospholenes[4] (I) to the carbonyl group of mono- and polycarbonyl compounds constitutes a new and a stereoselective method of making carbon–carbon bonds. This reaction, which can be conveniently named the *oxyphosphorane condensation*,[3] produces derivatives of the 2,2-dihydro-1,3,2-dioxaphospholane ring system, II.



I II

(1) Part XXXVIII: Organic Compounds with Pentavalent Phosphorus.

(2) This investigation was supported by Public Health Service Grant CA-04769 from the National Cancer Institute and by the National Science Foundation, Grants GP-3341 and GP-6690-Y.

(3) (a) F. Ramirez and N. Ramanathan, *J. Org. Chem.*, **26**, 3041 (1961); (b) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Amer. Chem. Soc.*, **84**, 1317 (1962); (c) F. Ramirez, *Pure Appl. Chem.*, **9**, 337 (1964); (d) F. Ramirez, *Bull. Soc. Chim. Fr.*, 2443 (1966).

(4) Derivatives of the 2,2-dihydro-1,3,2-dioxaphospholenes like III were first described by three groups of investigators: (a) G. H. Birum and J. L. Dever, Abstracts, Division of Organic Chemistry, 135th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1958, p 101-P; (b) V. A. Kukhtin, *Dokl. Akad. Nauk SSSR*, **121**, 466 (1958); *Chem. Abstr.*, **53**, 1105*b* (1959); (c) F. Ramirez and N. B. Desai, *J. Amer. Chem. Soc.*, **82**, 2650 (1960). Our discovery of phospholenes III from the reactions of trialkyl phosphites with *o*-quinones and α-diketones was based on our previous discovery of the attack by the phosphorus of trialkyl phosphites on the oxygen of *p*-quinones: *cf.* (d) F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 856 (1957); (e) F. Ramirez and S. Dershowitz, *ibid.*, **23**, 778 (1958).