α-Phosphoryl Sulfoxides. 3. Dimethylphosphorylmethyl p-Tolyl Sulfoxide. Resolution, Stereospecific Synthesis, and the Horner–Wittig Reaction. A New Synthesis of Optically Active α,β-Unsaturated Sulfoxides[1]

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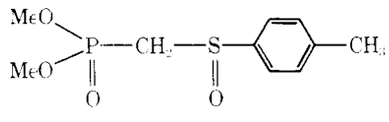
As part of a continuing study of α-phosphoryl sulfoxides, racemic dimethylphosphorylmethyl p-tolyl sulfoxide (1) was prepared and resolved into optical isomers via fractional crystallization of diastereomeric quininium salts of methyl-p-tolylsulfinylmethylphosphonic acid (5) and subsequent methylation of the tetramethylammonium salts of the resulting enantiomers of 5. Sulfoxide (+)-1 with the *R* chirality at sulfur was synthesized stereospecifically by treatment of (−)-(*S*)-menthyl p-tolylsulfinate (2) with dimethylphosphorylmethyllithium (4). The enantiomeric and optical purity of chiral sulfoxides 1 was determined by means of NMR spectroscopy using a chiral europium shift reagent. It was demonstrated that the lithio derivative of (+)-1 reacted with a variety of carbonyl compounds to afford optically active α,β-unsaturated sulfoxides. In some cases the formation of β,γ-unsaturated sulfoxides was observed.

α-Phosphoryl sulfoxides[2-4] are of considerable interest from both synthetic and stereochemical points of view. Like simple sulfoxides, they undergo the Pummerer and Pummerer-type reactions, halogenation, oxidation, and reduction.[5] Owing to the presence of the phosphonate moiety, α-phosphoryl sulfoxides are key substrates in the synthesis of α,β-unsaturated sulfoxides based on the Horner–Wittig reaction.[3] It should be mentioned that this reaction can be also carried out in a catalytic two-phase system in which the α-phosphoryl sulfoxides act as phase-transfer catalysts.[6-8]

Although a number of methods for preparing α,β-unsaturated sulfoxides are known,[9] synthetic approaches to their optically active analogues are few in number and for the most part of limited applicability. The majority of optically active, α,β-unsaturated sulfoxides described in the chemical literature have been prepared according to Andersen's procedure from a reaction of (−)-menthyl p-tolylsulfinate with vinyl Grignard reagents.[10] Tschuchihashi et al.[11] obtained the isomer *E* of optically active styryl p-tolyl sulfoxide by condensation of (+)-(*R*)-methyl p-tolyl sulfoxide with benzaldehyde followed by elimination of water. A method described by Naso et al.[12] consisting of an asymmetric elimination of β-haloethyl p-tolyl sulfoxides by optically active amines is interesting but not very useful in practice since it affords vinyl p-tolyl sulfoxide with an optical purity of less than 20%.

Therefore, with the intent of developing a general method for the synthesis of optically active α,β-unsaturated sulfoxides, we have prepared optically active α-phosphoryl sulfoxides with the optically active center at the sulfur atom. In this paper we describe the synthesis of optically active dimethylphosphorylmethyl p-tolyl sulfoxide (1) and its Horner–Wittig reaction with carbonyl compounds. This sulfoxide was chosen because of the possibility of correlating its configuration with



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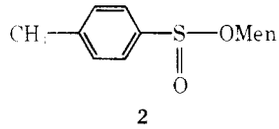

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(−)-(*S*)-menthyl p-tolylsulfinate (2) which is a common precursor to many optically active sulfinyl compounds.[13,16]

Results and Discussion

Synthesis of Racemic Dimethylphosphorylmethyl p-Tolyl Sulfoxide (1) and Its Enantiomers via Optical Resolution. Racemic sulfoxide 1 was prepared in good yields by a selective oxidation of dimethylphosphorylmethyl p-tolyl sulfide (3) with sodium metaperiodate and by the reaction of the lithio derivative of dimethyl methylphosphonate (4) with methyl p-tolylsulfinate.

The presence of the phosphonate moiety in the molecule of sulfoxide 1 offers the possibility of its utilization not only in the Horner–Wittig reaction but also for the transformation of the phosphonate ester function into the corresponding phosphonic acid 5, which in turn makes possible the resolution of the chiral sulfoxide grouping by the classical method via diastereomeric salts with optically active amines. For this reason we prepared methyl p-tolylsulfinylmethylphosphonic acid (6) by two methods. In one of them sulfide 3 was used as the starting material. We found that it was readily demethylated by reaction with sodium iodide at 130–150 °C or hydrolyzed under alkaline conditions (12% aqueous NaOH–dioxane) to give the sodium salt of *O*-methyl p-tolylthiomethylphosphonic acid (6). The dicyclohexylammonium salt of this acid (mp 132–132.5 °C) was oxidized to the dicyclohexylammonium salt of 5 (mp 152.5–153.5 °C) from which the free acid 5 having mp 94–95 °C was liberated by passing it through an ion-exchange column.

An alternative route to 5 involved the direct alkaline hydrolysis of sulfoxide 1 which resulted in the formation of the desired product in 75% yield.

Racemic acid 5 readily formed a crystalline quinine salt, $[\alpha]_D$ −78°, which after six crystallizations from acetone afforded in 19% yield the diastereomeric salt having $[\alpha]_D$ −186°. Its specific rotation remained unchanged after further crystallizations. Decomposition of this salt gave the free acid (−)-5, $[\alpha]_D$ −142°. The more soluble diastereomeric salt having $[\alpha]_D$ −3.9° was isolated from the acetone mother liquors in 47% yield. After acidification of this salt (−)-5, $[\alpha]_D$ +103°, was obtained. Both antipodes of acid 5 were converted into their tetramethylammonium salts and treated with methyl iodide in acetonitrile to give the enantiomeric sulfoxides 1 with $[\alpha]_D$ −149° and +106°, respectively. The experiments described above are shown in Scheme I.

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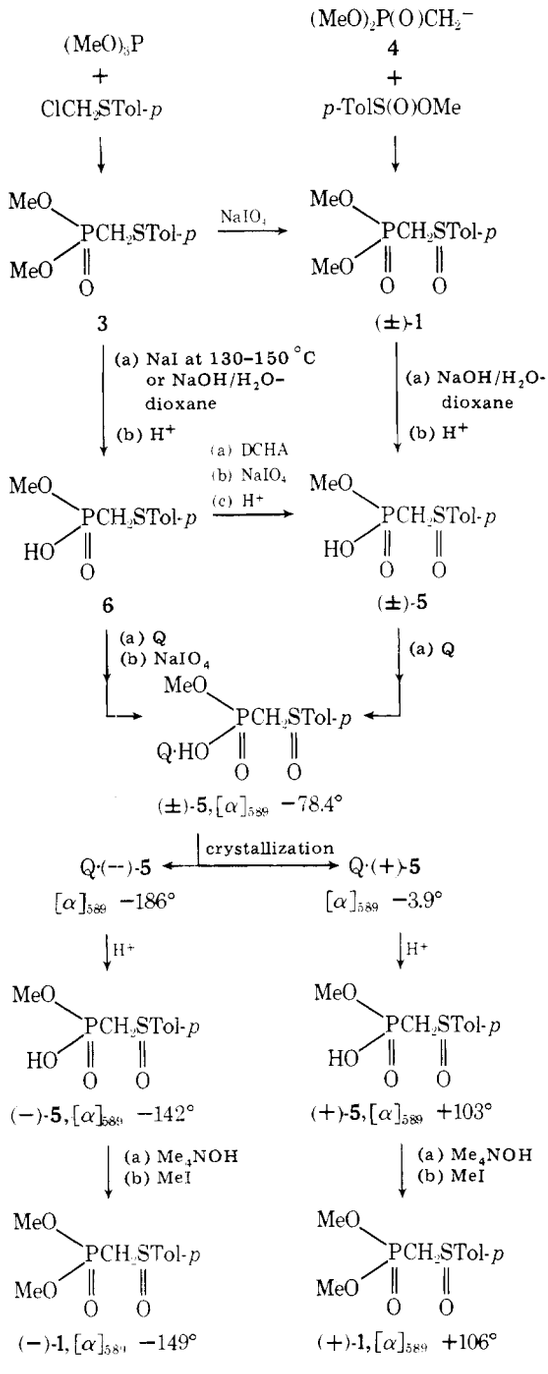
Scheme I. Synthesis of Racemic and Optically Active Dimethylphosphorylmethyl *p*-Tolyl Sulfoxide (1)



DCHA - dicyclohexylamine; Q - quinine.

It is worthwhile to mention that our approach to optically active sulfoxides 1 is general and can be applied to any α-phosphoryl sulfoxide.

Determination of the Enantiomeric and Optical Purity of α-Phosphoryl Sulfoxide 1 by NMR. Resolution is often deemed complete once the enantiomers are obtained with equal and opposite specific rotations. This criterion, however, has limited precision and since in our case it was not fulfilled, an independent establishment of the optical purity of enantiomeric sulfoxides 1 was desirable. We employed, therefore, a chiral lanthanide shift reagent, tris-[3-(trifluoromethylhydroxymethylene)-*d*-camphorato]europium(III), (TFMC),[14] as a chiral medium for separation of the enantiomeric resonances of sulfoxide 1.

However, before these experiments are considered, it is

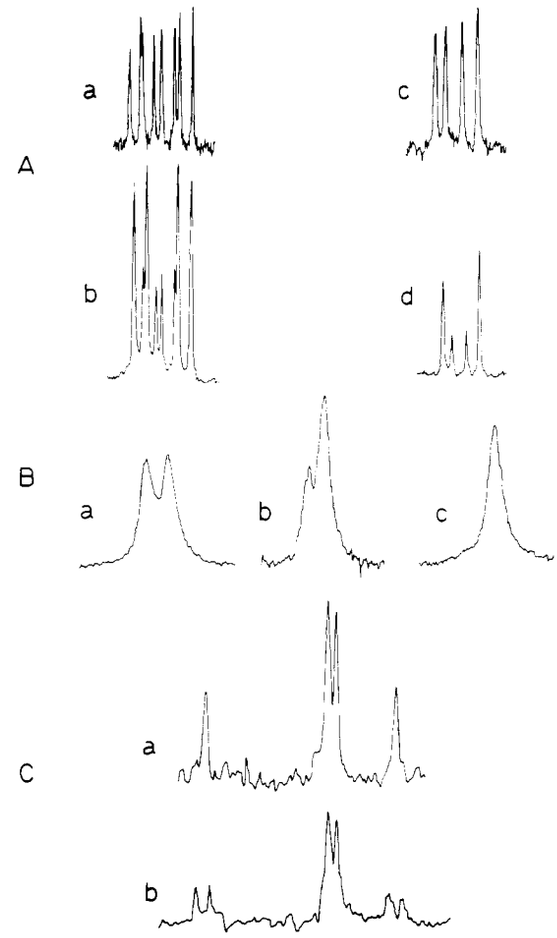
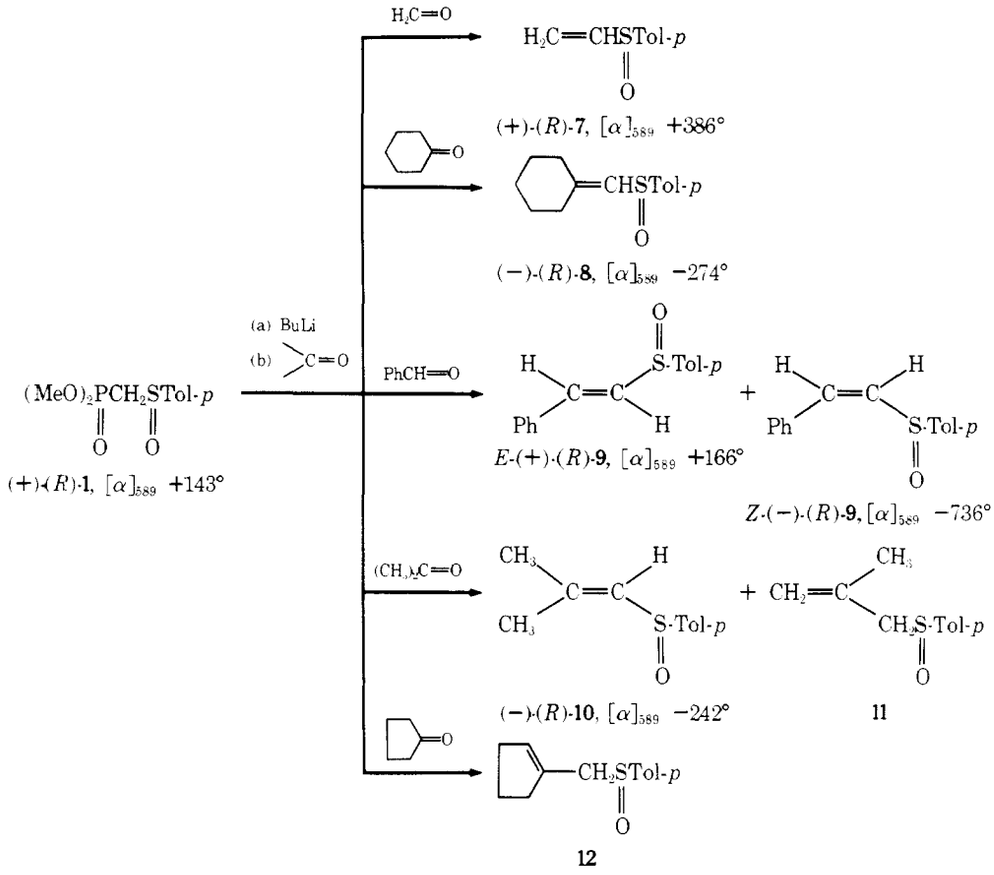


Figure 1. ^{1}H NMR (A), ^{31}P NMR (B), and ^{13}C NMR (C) spectra of sulfoxide 1 in the presence of chiral shift reagent TFMC. The ratio of 1 to TFMC was 1:2, chloroform as solvent was used. (A) Normal (a and b) and phosphorus decoupled (c and d) resonance signals of the methoxy protons: (a) (±)-1 and TFMC; (b) (+)-1, $[\alpha]_D$ +50.4°, and TFMC. (B) Proton decoupled ^{31}P NMR spectra. (a) (±)-1 and TFMC ($\Delta\delta$ = 21 Hz); (b) (−)-1, $[\alpha]_D$ −74.5°, and TFMC; (c) (−)-1, $[\alpha]_D$ −149°, and TFMC. (C) Proton decoupled ^{13}C NMR resonance signals of the methylene and methoxy carbons. (a) (±)-1 without TFMC; (b) (±)-1 in the presence of TFMC ($\Delta\delta$ = 9.8 Hz).

appropriate to describe the ^{1}H NMR spectrum of sulfoxide 1. Thus, the ^{1}H NMR spectrum of 1 at 90 MHz showed, in addition to the resonance signals of the *p*-tolyl protons (singlet at δ 2.42 ppm and multiplet at δ 7.48 ppm), two doublets centered at δ 3.74 and 3.80 ppm ($J_{CH_3\text{-}P}$ = 11 Hz) which correspond to the diastereotopic methoxy groups as well as two AB systems at δ 3.29 and 3.40 ppm which are a part of the ABX system (X = phosphorus) and correspond to the nonequivalent methylene protons. It is obvious that the chiral sulfur atom in 1 induces the magnetic nonequivalence of the methoxy and methylene protons.

The ^{1}H NMR spectrum of racemic 1 in the presence of TFMC revealed further doubling of the methoxy resonance signals whereas no separation of the enantiomeric resonances was observed for the other groups of protons. Therefore, only the methoxy signals are of analytical value. As expected, the ^{1}H NMR spectrum of (+)-1, $[\alpha]_D$ +50.4°, in the presence of TFMC contained two pairs of the methoxy doublets of different intensity. The integration of these signals provided the basis for the determination of the enantiomeric (+)-1/(−)-1 ratio as 67.6:32.4 and an estimation of the specific rotation for optically pure sulfoxide 1. The calculated value was equal to $[\alpha]_D$ +143° which is in good agreement with the experimental value obtained for (−)-1 (the difference lies within the limits of error of the NMR determination). With regard to the ac-

Scheme II. The Horner–Wittig Reaction of (+)-(*R*)-Dimethylphosphorylmethyl *p*-Tolyl Sulfoxide (1) with Aldehydes and Ketones



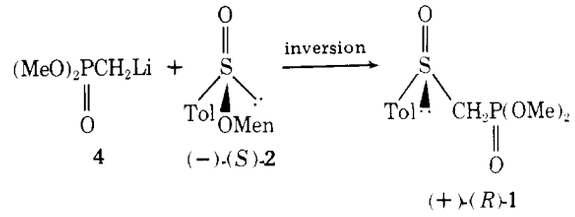
curacy of the NMR method, the phosphorus decoupled ^1H NMR spectra proved to be very useful.

The ^{31}P NMR spectra were also utilized to demonstrate that sulfoxide (−)-1, $[\alpha]_D$ −149°, was optically pure. In the proton decoupled ^{31}P NMR spectrum of a mixture of racemic 1 with TFMC, there were observed two well separated singlets of equal intensity due to enantiomeric sulfoxides 1. Since in the $^{31}P\{H\}$ NMR spectrum of (−)-1, $[\alpha]_D$ −149° in the presence of TFMC there was only one singlet, it can be assumed that the examined sample is optically pure.

It is also of special interest to note that in the $^{13}C\{H\}$ NMR spectrum of sulfoxide 1 with TFMC, the separation of the enantiomeric resonances of the methylene carbon was observed. The ^1H, ^{31}P, and ^{13}C NMR spectra discussed above are shown in Figure 1.

Stereospecific Synthesis of (+)-(*R*)-Dimethylphosphorylmethyl *p*-Tolyl Sulfoxide (1). Although the synthesis of both enantiomers of 1 has been accomplished, the method involving optical resolution of diastereomeric quininium salts of acid 5 followed by methylation is not very satisfactory for two reasons; i.e., the total yield of enantiomeric sulfoxides 1 obtained by this procedure was not satisfactory, and the dextrorotatory isomer of 1 was obtained in only 70% optical purity. Therefore, to overcome these limitations we extended our study to the reaction of phosphonate carbanions with sulfinic esters (reported by us earlier).[4] We have now found that treatment of (−)-(*S*)-menthyl *p*-tolylsulfinate (2), $[\alpha]_D$ −202°, with two moles of dimethylphosphorylmethyllithium (4) at −20 °C in tetrahydrofuran gave the sulfoxide (+)-1, $[\alpha]_D$ +144° in about 70% yield.[15]

Surprisingly, this reaction resulted in the formation of the dextrorotatory sulfoxide 1 which was almost optically pure. In view of this finding, the two methods may be considered to be complementary.



The reaction described above also allowed us to assign the absolute configuration to enantiomeric sulfoxides 1. Since this reaction is a typical nucleophilic substitution at sulfinyl sulfur and undoubtedly takes place with inversion of configuration at sulfur,[16] it is reasonabe to assume that the chirality at sulfur in sulfoxide (+)-1 is *R*.

Synthesis of Optically Active α,β-Unsaturated Sulfoxides. Since a method for synthesizing enantiomeric sulfoxides 1 was now available, the remaining problem was to apply it for the synthesis of optically active α,β-unsaturated sulfoxides. The reaction of the lithio derivative of sulfoxide (+)-(*R*)-1, $[\alpha]_D$ +143°, with carbonyl compounds was carried out under conditions similar to those described previously[3] for racemic diethylphosphorylmethyl methyl sulfoxide. The results obtained from reaction of the organolithium reagent with formaldehyde, cyclohexanone, benzaldehyde, acetone, and cyclopentanone are summarized in Scheme II.

The reaction of (+)-(*R*)-1 with formaldehyde gave (+)-vinyl *p*-tolyl sulfoxide (7), $[\alpha]_D$ +386° which is known to have the *R* chirality at sulfur.[10]

Taking into account the fact that the Horner–Wittig reaction of (+)-1 does not disturb the configuration at the chiral sulfur, this result provides independent proof of correctness of our configurational assignments to the enantiomers of sulfoxide 1. The reaction with cyclohexanone yielded sulfoxide (−)-(*R*)-8, $[\alpha]_D$ −274°.

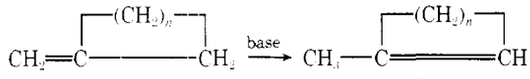
As expected, in the case of the reaction of benzaldehyde, a mixture of isomers $E + Z$ of styryl p-tolyl sulfoxide (R)-(**9**) in the ratio 75:25 was obtained. The specific rotation of the product was found to be $[\alpha]_D$ −68°. Since the isomer E of sulfoxide (R)-**9** is dextrorotatory and its specific rotation value reported in the literature[11] is $[\alpha]_D$ +164.5°, the negative sign of the specific rotation of our product must have been due to a very high rotation value of the isomer Z-(R)-**9** of opposite sign. It is noteworthy that the pure Z isomer of optically active sulfoxide **9** has not yet been prepared and characterized. Therefore, by means of column chromatography the initially obtained mixture of sulfoxides (R)-**9** was separated into the pure E and Z isomers having $[\alpha]_D$ +166° and −736°, respectively. We would like to point out that, although the chirality at sulfur in both geometrical isomers is the same, the signs of their specific rotation are opposite.

Analysis of the ^{1}H NMR spectrum of the crude product upon reaction of (+)-(R)-**1** with acetone revealed the presence of two olefinic compounds separable by column chromatography. The major product was the expected (−)-(R) 1-(p-tolylsulfinyl)-2-methylpropene (**10**), $[\alpha]_D$ −242° whereas the minor product has been identified as 2-methylallyl p-tolyl sulfoxide (**11**), i.e., the isomeric β,γ-unsaturated system. The ratio of α,β- to β,γ-unsaturated isomers **10** and **11** was found by NMR spectral analysis to be 66:34. In the case of cyclopentanone the only product obtained was β,γ-unsaturated sulfoxide **12**.[17]

Although the base-catalyzed isomerization of α,β- to β,γ-unsaturated isomers of alkenyl methyl sulfides, sulfoxides, and sulfones is well known,[18] this seems to be the first reported case of it occurring under the Horner–Wittig reaction conditions.[19] It is quite likely that the initially formed α,β-unsaturated sulfoxides undergo isomerization to the corresponding β,γ isomers under the basic reaction conditions especially in view of the fact that a small molar exesss in n-butyllithium was used for the generation of **4**.[20]

$$RCH_2CH{=}CHS(O)R \overset{\text{base}}{\rightleftharpoons} RCH{=}CHCH_2S(O)R$$

The isomerization rate depends on the structure of the particular sulfoxide. The exclusive formation of the β,γ-unsaturated sulfoxide **12** prepared from cyclopentanone and the stability of α,β-unsaturated sulfoxide **8** prepared from cyclohexanone are not surprising. Thus the activation parameters for the base-catalyzed isomerization of methylenecycloalkanes to methylcycloalkenes are $H^{\ddagger}$ = 13.3 kcal/mol and $S^{\ddagger}$ = −17 eu for five-membered systems, and $H^{\ddagger}$ = 27.1 kcal/mol and $S^{\ddagger}$ = 0.7 eu for six-membered systems.[21]



Finally, a comment regarding the optical activity of sulfoxides **11** and **12**; i.e., on isolation, both sulfoxides exhibited very small positive rotations. Like other optically active allyl sulfoxides, they most probably undergo fast racemization by a [2,3]sigmatropic process to give the achiral sulfenate ester as an intermediate.[22]

Experimental Section

All melting and boiling points are uncorrected. Solvents and commerical reagents were distilled and dried by conventional methods before use. ^{1}H NMR spectra were recorded at 60 MHz with a R12B Perkin-Elmer spectrometer and at 90 MHz with a Bruker HX90 spectrometer. ^{31}P and ^{13}C NMR spectra were obtained on a Jeol JNM-C-60 H1 spectrometer with external H_3PO_4 and internal Me_4Si as the standards, respectively. Column chromatography was done on Merck silica gel, 100–200 mesh. Optical activity measurements were made with a Perkin-Elmer 241 MC photopolarimeter in chloroform solution, unless specified otherwise.

Dimethylphosphorylmethyl p-Tolyl Sulfide (3). A mixture of chloromethyl p-tolyl sulfide (51.3 g, 0.3 mol) and trimethyl phosphite was heated at 150–160 °C for 10 h. The crude product was distilled to give **3** as a colorless oil: bp 120–122 °C (0.05 mmHg), n^{20}D 1.5472, 51.7 g (70%); ^{1}H NMR ($CDCl_3$) δ 2.3 (s, 3, $CH_3C_6H_4$), 3.15 (d, 2, CH_2–P(O), $^1J_{P\text{-}CH_2}$ = 14 Hz), 3.74 (d, 6, CH_3OP, $^2J_{P\text{-}CH_3}$ = 10.7 Hz), 7.13 and 7.37 (A_2B_2 system, 4, aromatic, J_{AB} = 8.3 Hz); ^{31}P NMR ($CHCl_3$) δ −26.3. Anal. Calcd for $C_{10}H_{15}O_3PS$: C, 48.77; H, 6.14; P, 12.57. Found: C, 49.12; H, 6.38; P, 12.42.

Oxidation of Sulfide 3 to Dimethylphosphorylmethyl p-Tolyl Sulfoxide (1). To a solution of sulfide **3** (2.46 g, 0.01 mol) in 13 mL of acetone and 7 mL of water a solution of sodium metaperiodate (2.25 g, 0.0105 mol) in water was added within 1 h at −5 to 0 °C. The reaction mixture was stirred at 0 °C for 4 h and allowed to stand at 5 °C for 24 h. The precipitated sodium iodate was filtered off. After removal of acetone the water solution was extracted with chloroform (5 × 10 mL). The chloroform extract was dried over anhydrous $MgSO_4$ and evaporated to give pure sulfoxide **1** as a colorless oil: n^{23}D 1.5295, 2.49 g (95%); ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3, CH_3–C_6H_4), 3.29 and 3.40 (AB part of ABX system, 2, $CH_2P(O)$, J_{AB} = 14.55 Hz, J_{AX} = 14.65 Hz, J_{BX} = 15.43 Hz, X = phosphorus); 3.74 and 3.80 (dd, 6, CH_3OP, $^2J_{P\text{-}CH_3}$ = 11.52 and 10.94 Hz); 7.48 (A_2B_2 system, 4, aromatic); ^{13}C NMR ($CHCl_3$) δ 21.28 (s, CH_3–C_6H_4), 53.89 (d, CH_2–P, $J_{P\text{-}CH_2}$ = 137.9 Hz), 52.99 (d, CH_3OP, $^2J_{CH_3\text{-}P}$ = 6.10 Hz); 124.10, 129.95 and 142.2 (aromatic carbons); ^{31}P NMR ($CHCl_3$) δ −20.8. Anal. Calcd for $C_{10}H_{15}O_4PS$: C, 45.79; H, 5.77; P, 11.91. Found: C, 46.14; H, 5.93; P, 11.74.

Reaction of Methyl p-Tolylsulfinate with Lithium Dimethyl Methylphosphonate (4). To a solution of dimethyl methylphosphonate (2.48 g, 0.02 mol) in THF (30 mL) a solution of n-butyllithium (16 mL, 0.022 mol) in hexane was added at −78 °C under a nitrogen atmosphere. The reaction mixture was stirred at this temperature for 0.5 h and then a solution of methyl p-tolyl sulfinate (1.70 g, 0.01 mol) in THF (20 mL) was added. Stirring at −78 °C was continued for 15 min. The mixture was warmed slowly to −20 °C and quenched with aqueous ammonium chloride. After evaporation of THF and hexane, the aqueous layer was extracted with chloroform (3 × 25 mL). The chloroform solution was dried and evaporated to give a crude oil from which excess dimethyl methylphosphonate was distilled (0.01 mmHg). Dimethylphosphorylmethyl p-tolyl sulfoxide (**1**) obtained in this manner (2.1 g, 80%) was chromatographed [benzene–acetone (5:1)] to afford the analytically pure sulfoxide **1**. Anal. Calcd for $C_{10}H_{15}O_4PS$: C, 45.79; H, 5.77; P, 11.81. Found: C, 45.62; H, 5.64; P, 11.70. The NMR spectra were identical with those recorded for **1** described above.

Synthesis of Methyl p-Tolylthiomethylphosphonic Acid (6). A. Demethylation of Sulfide 3. A mixture of **3** (24.6 g, 0.1 mol) and sodium iodide (15 g, 0.1 mol) was heated for 3 h at 140–150 °C. The resulting sodium salt of acid **6** was dissolved in water (150 mL). The water solution was extracted with chloroform (2 × 25 mL) in order to remove neutral impurities. The aqueous layer was acidified and extracted with chloroform (5 × 25 mL). After drying over anhydrous $MgSO_4$ and evaporation of the chloroform solution, 14.1 g (61%) of acid **6** as a pale yellow oil, n^{21}D 1.5615, was obtained. It was characterized as dicyclohexylammonium salt (see below).

B. Alkaline Hydrolysis of Sulfide 3. To a solution of **3** (7.38 g, 0.03 mol) in dioxane (30 mL) sodium hydroxide (3.6 g) in 10 mL of water was added. The reaction mixture was stirred at room temperature for 2 h. After neutralization and removal of dioxane, an aqueous layer was washed with chloroform (25 mL), acidified, and then extracted with chloroform (5 × 25 mL). The chloroform solution obtained after extraction of the acidic aqueous layer was dried and concentrated to give 4.18 g (60%) of acid **6**: n^{22}D 1.5617; ^{1}H NMR ($CDCl_3$) δ 2.25 (s, 3, CH_3–C_6H_4), 3.1 (d, 2, CH_2–P, $^1J_{P\text{-}CH_2}$ = 14.7 Hz), 3.67 (d, 3, CH_3OP, $^2J_{P\text{-}CH_3}$ = 12 Hz), 7.17 (A_2B_2 system, 4, aromatic); ^{31}P NMR ($CHCl_3$) δ −26.9. Anal. Calcd for $C_9H_{13}O_3PS$: C, 46.54; H, 5.64; P, 13.34. Found: C, 46.31; H, 5.73; P, 13.39.

Dicyclohexylammonium Salt of Acid 6. Compound **6** [2.78 g (0.012 mol)] was mixed with dicyclohexylamine (2.17 g, 0.012 mol). The resulting crystalline salt was washed with ether and recrystallized from acetone to yield 4.14 g (83.7%) of the desired salt: mp 132–132.5 °C; ^{31}P NMR ($CHCl_3$) δ −14.7. Anal. Calcd for $C_{21}H_{36}O_3NPS$: C, 60.99; H, 8.77; N, 3.39; P, 7.49. Found: C, 60.80; H, 8.81; N, 3.40; P, 7.57.

Quininium Salt of Acid 6. To a solution of free acid **6** (5.2 g, 0.0224 mol) in acetone an equimolar amount of quinine (8.48 g) was added. The product was recrystallized from acetone to give 12.24 g (89%) of the title salt, mp 56–57 °C $[\alpha]_D$ −99° (c, 1.7; chloroform); ^{31}P NMR ($CHCl_3$) δ−17.2 Anal. Calcd for $C_{29}H_{39}O_6N_2PS$: C, 60.84; H, 6.84; P, 5.39. Found: C, 60.91, H, 6.72; P, 5.37.

Synthesis of Methyl *p*-Tolylsulfinylmethylphosphonic Acid (5). A. Oxidation of Dicyclohexylammonium Salt of 6. To a solution of the salt (4.13 g, 0.01 mol) in water and acetone sodium metaperiodate (2.25 g, 0.0105 mol) in water was added dropwise at −5 to 0 °C. Stirring at 0 °C was continued for 3 h and the reaction mixture was allowed to stand at 0 °C overnight. After evaporation of acetone, the dicyclohexylammonium salt of acid **5** was extracted with chloroform (4 × 25 mL). The chloroform extract was dried over $MgSO_4$ and the solvent was evaporated to give the required salt which was purified by crystallization from acetone: mp 152–153.5 °C; 3.48 g (81%), ^{31}P NMR ($CHCl_3$) δ −7.9. Anal. Calcd for $C_{21}H_{36}O_4NPS$: C, 58.72; H, 8.45; N, 3.26; P, 7.21. Found: C, 59.27; H, 8.59; N, 3.28; P, 7.31.

Dicyclohexylammonium salt (2.145 g, 0.005 mol) prepared as above was passed through an ion-exchange column (Dowex 50W-X1). After evaporation of water and drying 1.23 g (100%) of a free acid **5** was obtained: mp 94–95 °C; ^1H NMR ($CDCl_3$) δ 2.4 (s, 3, CH_3–C_6H_4), 3.41 (d, 2, CH_2–P(O), $^1J_{P\text{-}CH_2}$ = 14.7 Hz), 3.7 (d, 3, CH_3OP, $^2J_{P\text{-}CH_3}$ = 11.3 Hz), 7.42 (A_2B_2 system, 4, aromatic); ^{31}P NMR ($CHCl_3$) δ −17. Anal. Calcd for $C_9H_{13}O_4PS$: C, 43.54; H, 5.28; P, 12.48. Found: C, 43.43; H, 5.27; P, 12.38.

B. Alkaline Hydrolysis of Sulfoxide 1. To a solution of sulfoxide **1** (3.93 g, 0.015 mol) in 30 mL of dioxane a solution of sodium hydroxide (1.8 g, 0.045 mol) in 15 mL of water was added dropwise. The reaction mixture was stirred for 2 h at room temperature and treated then with 50 mL of water. After evaporation of dioxane, the aqueous layer was washed with chloroform, acidified with hydrochloric acid, and washed once with chloroform. On evaporation of water the residue was extracted with chloroform (5 × 25 mL). The solvent was evaporated to give 2.82 g (75.7%) of acid **5**, physical and spectral properties of which were identical with those described above.

Oxidation of Quininium Salt of Acid 6. To a solution of quininium salt of **6** (12.21 g, 0.02 mol) in acetone and water a solution of sodium metaperiodate (4.49 g, 0.021 mol) in water (75 mL) was dropped below 0 °C. The reaction mixture was stirred for 4 h at 0 °C and the resulting quininium salt of acid **5** was isolated by extraction with chloroform (5 × 25 mL) and the usual work-up: 11.6 g (93%), mp 50–57 °C; $[\alpha]_D$ −75° (*c* 1.7 $CHCl_3$); ^{31}P NMR ($CHCl_3$) δ −10.4. Anal. Calcd for $C_{29}H_{41}O_8N_2PS$: C, 55.58; H, 6.92; P, 4.94. Found: C, 55.94; H, 6.29; P, 5.01.

Quininium Salt of Acid 5. Alternatively, the title salt was prepared by mixing acid **5** (0.248 g, 0.001 mol) and quinine (0.3785 g, 0.001 mol) in acetone (15 mL). Evaporation of the solvent yielded 0.6265 g of the desired salt: mp 52–59 °C $[\alpha]_D$ −78.4° (*c* 1.55, $CHCl_3$).

The Resolution of Methyl *p*-Tolylsulfinylmethylphosphonic Acid (5) via Quininium Salt. The title salt (6.26 g) was crystallized from acetone (750 mL). On cooling, 1.75 g of salt, $[\alpha]_D$ −147° (*c* 1.8, $CHCl_3$) was collected, then recrystallized five times from acetone to give 1.18 g (19%) of a diastereomeric head crop, mp 181–182 °C $[\alpha]_D$ −186° (*c* 1.9, $CHCl_3$), ^{31}P NMR ($CHCl_3$) δ −10.4. This salt on passing through the ion-exchange column gave 0.465 g of acid (−)-**5**, $[\alpha]_D$ −142° (*c* 1.2, $CHCl_3$).

The mother liquor was concentrated and the residue was recrystallized from acetone to afford a salt $[\alpha]_D$ −43° (*c* 1.7, $CHCl_3$). Subsequent recrystallizations of this salt from acetone–ether (2:1) yielded 2.96 g (47%) of the salt $[\alpha]_D$ −3.9° (*c* 1.65, $CHCl_3$), the rotation of which remained unchanged after further crystallizations. The acid (+)-**5** (0.947 g) recovered from this salt has $[\alpha]_D$ +103° (*c* 1.31, $CHCl_3$)

Optically Active Sulfoxide (−)-1. Acid (−)-**5**, $[\alpha]_D$ −142° (0.232 g, 0.000935 mol) was dissolved in water (50 mL) and neutralized with a 25% aqueous solution of tetramethylammonium hydroxide. On evaporation, the tetramethylammonium salt of acid (−)-**5** was obtained, ^{31}P NMR ($CHCl_3$) δ −8.5.

The above prepared salt (0.323 g) was refluxed for 2 h with an excess of methyl iodide in acetonitrile (50 mL). After removal of the solvent, the residue was dissolved in water (40 mL) and extracted with chloroform (5 × 10 mL). The chloroform solution was evaporated to give the crude sulfoxide (−)-**1** which was purified by column chromatography using benzene–acetone (5:1) as the eluent. (−)-**1**, $[\alpha]_D$ −149° (*c* 1.16, acetone), 0.156 g (62.5%). Anal. Calcd for $C_{10}H_{15}O_4PS$: C, 45.79; H, 5.77; P, 11.91. Found: C, 46.07; H, 5.84; P, 11.59.

Optically Active Sulfoxide (+)-1. Similarly, (+)-**1**, $[\alpha]_D$ +106° (*c* 1.7, acetone) was prepared from (+)-**5**, $[\alpha]_D$ +103° (*c* 1.31, $CHCl_3$) in 61.5% yield.

Preparation of Sulfoxide (+)-(R)-1 from (−)-(S)-Menthyl *p*-tolylsulfinate (2). To a solution of the lithium derivative of dimethyl methylphosphonate (0.02 mol) prepared as described above a solution of (−)-(S)-menthyl *p*-tolylsulfinate (2.94 g, 0.01 mol), $[\alpha]_D$ −202° (*c* 1.2, acetone) in 20 mL of THF was added at −78 °C. After 15 min the reaction mixture was warmed to −20 °C and quenched with aqueous ammonium chloride. After evaporation of the organic solvents (THF, hexane) the aqueous layer was extracted with petroleum ether (to remove menthol) and then with chloroform (3 × 25 mL). The chloroform solution was dried and evaporated. Careful removal of dimethyl methylphosphonate under reduced pressure gave 1.87 g (72%) of (+)-(*R*)-**1**. The analytically pure sample of this sulfoxide, $[\alpha]_D$ +144° (*c* 1.0, acetone), was obtained after column chromatography using benzene–acetone (5:1) as the eluent. Anal. Calcd for $C_{10}H_{15}O_4PS$: C, 45.79; H, 5.77; P, 11.81. Found: C, 45.53; H, 5.71; P, 11.72.

Synthesis of Optically Active α,β-Unsaturated Sulfoxides and β,γ-Unsaturated Sulfoxides from (+)-(*R*)-1 and Carbonyl Compounds. All the sulfoxides listed in Scheme III were obtained according to the general procedure for the Horner–Wittig reaction of diethylphosphorylmethyl methyl sulfoxide with carbonyl compounds described previously.[3] The isolation procedure as well as the physical and spectral data of sulfoxides **7–12** follow.

(+)-(*R*)-*p*-Tolylsulfinylethylene (7). Column chromatography [benzene–acetone (200:3)] of the crude product from paraformaldehyde (0.15 g, 0.005 mol) and sulfoxide (+)-(*R*)-**1** (1.31 g, 0.005 mol), $[\alpha]_D$ +143°, gave 0.62 g (75%) of sulfoxide (+)-(*R*)-**7**, $[\alpha]_D$ +386° (*c* 0.98, ethanol), n^{25}_D 1.5747; ^1H NMR ($CDCl_3$) δ 2.28 (s, 3, CH_3–C_6H_4), 5.70–6.78 (m, 3, —CH=CH_2, ABC system), 7.35 (m, 4, aromatic). Anal. Calcd for $C_9H_{10}OS$: C, 65.10; H, 6.00. Found: C, 65.01; H, 6.11.

(−)-(*R*)-1-[(*p*-Tolylsulfinyl)methylene]cyclohexane (8). The reaction of cyclohexanone (0.49 g, 0.005 mol) and (+)-**1** was carried out according to the standard procedure and the crude product was chromatographed [benzene–acetone (200:3)] to give 0.935 g (80%) of (−)-(*R*)-**8**, $[\alpha]_D$ −272° (*c* 0.85, acetone); ^1H NMR δ 1.62 [m, 6, $(CH_2)_2CH_2$-], 2.22 [m, 4, $(CH_2)_2C$=], 2.38 (s, 3, CH_3–C_6H_4), 5.94 (s, 1, CH=C-), 7.37 (m, 4, aromatic). Anal. Calcd for $C_{14}H_{18}OS$: C, 71.75; H, 7.74. Found: C, 71.98; H, 7.85; n^{22}_D 1.5610.

Styryl *p*-Tolyl Sulfoxide (9). The crude product (1.15 g, 95%), $[\alpha]_D$ −68° (*c* 1.08, chloroform), obtained from benzaldehyde (0.56 g, 0.005 mol) was a mixture of *E* and *Z* isomers in a ratio of 69:31. Column chromatography [benzene–acetone (200:3)] afforded both pure geometrical isomers of the title sulfoxide.

(*E*)-(+)-(*R*)-**9**: $[\alpha]_D$ +166° (*c* 1.14, chloroform); mp 82 °C; ^1H NMR ($CDCl_3$) δ 2.37 (s, 3, CH_3–C_6H_4), 6.72 (part of AB system, 1, J_{AB} = 15.3 Hz), 7.16–7.56 (m, 10, aromatic and a part of AB system). Anal. Calcd for $C_{15}H_{14}OS$: C, 74.35; H, 5.82. Found: C, 74.37; H, 6.02.

(*Z*)-(−)-(*R*)-**9**: $[\alpha]_D$ −736° (*c* 1.04, chloroform), mp 52–52.5 °C; ^1H NMR ($CDCl_3$) δ 2.37 (s, 3, CH_3–C_6H_4), 6.38 and 7.04 (AB system, 2, vinyl protons, J_{AB} = 10.7 Hz), 7.16–7.58 (m, 9, aromatic). Anal. Calcd for $C_{15}H_{14}OS$: C, 74.35; H, 5.82; Found: C, 74.30; H, 5.88.

(−)-(*R*)-1(*p*-Tolylsulfinyl)-2-methylpropylene (10) and 2-Methylallyl *p*-Tolyl Sulfoxide (11). From acetone (0.29 g, 0.005 mol) and an equimolar amount of (+)-**1** the crude product was obtained as a pale yellow oil: 0.895 g (92%), $[\alpha]_D$ −80° (*c* 1.06, chloroform). It consisted of 76 and 24% of **10** and **11**, respectively. Column chromatography [benzene–acetone (200:3)] afforded pure α,β-unsaturated sulfoxide **10** and β,γ-sulfoxide **11** containing ca. 10% of impurities.

(−)-(*R*)-**10**: $[\alpha]_D$ −242° (*c* 1.29, chloroform), mp 65°C, 0.49 g (50.5%); ^1H NMR ($CDCl_3$) δ 1.88 and 2.16 (two s, 6H, $(CH_3)_2C$=), 2.38 (s, 3, CH_3–C_6H_4), 6.10 (s, 1, -CH-C=), 7.46 (m, 4, aromatic). Anal. Calcd for $C_{11}H_{14}OS$: C, 68.00; H, 7.26. Found: C, 68.11; H, 7.22.

11: 0.17 g (17.5%), ^1H NMR ($CDCl_3$) δ 1.80 (s, 3, CH_3-C=), 2.38 (s, 3, CH_3–C_6H_4), 3.30 and 3.53 (AB system, 2, -CH_2-S(O), J_{AB} = 10 Hz), 4.80 and 5.00 (two s, 2, CH_2=C), 7.50 (m, 4, aromatic).

1-*p*-Tolylsulfinylmethyl Cyclopentene (12). Cyclopentanone (0.42 g, 0.005 mol) and (+)-**1** gave, after the usual work-up, crude **12** (1.10 g, 100%) as a pale yellow oil. Column chromatography afforded 0.76 g (69%) of pure **12**: mp 48.5 °C; ^1H NMR ($CDCl_3$) δ 1.80–2.30 (m, 6, ring methylene protons), 2.35 (s, 3, CH_3–C_6H_4), 3.53 [broad s, 2, $CH_2S(O)$], 5.68 (broad s, 1, ring methine proton), 7.48 (m, 4, aromatic). Anal. Calcd for $C_{13}H_{16}OS$: C, 70.86; H, 7.32. Found: C, 70.63; H, 7.32.

Registry No.—(±)-**1**, 63231-19-6; (−)-**1**, 63268-43-9; (+)-(*R*)-**1**, 61187-71-1; (−)-(*S*)-**2**, 1517-82-4; **3**, 63231-20-9; **4**, 756-79-6; (±)-**5**, 63231-21-0; (±)-**5** DCHA, 63231-22-1; (−)-**5**, 63231-23-2; (−)-**5** Q, 63231-24-3; (−)-**5** Me_4N, 63231-26-5; (+)-**5**, 63231-27-6; (+)-**5** Q, 63301-42-8; **6**, 63231-28-7; **6** Na, 63231-29-8; **6** DCHA, 63231-30-1; **6** Q, 63231-31-2; (+)-(*R*)-**7**, 54828-68-1; (−)-*R*-**8**, 63231-32-3; (*E*)-(+)-(*R*)-**9**, 41103-85-9; (*Z*)-(−)-(*R*)-**9**, 63268-44-0; (−)-(*R*)-**10**, 63269-85-2; **11**, 37616-05-0; **12**, 63231-33-4; chloromethyl *p*-tolylsulfide, 34125-84-3; trimethyl phosphite, 121-45-9; methyl *p*-tolylsulfinate, 672-78-6; quinine, 130-95-0.

Table III. Solubility Corrections for Syn/Anti Dimer Ratios

p-XC_6H_4Br, X	Registry no.	0.1 mol % ArBr		10 mol % ArBr	
		Uncorrected	Corrected	Uncorrected	Corrected
H	108-86-1	4.96	4.96	1.10	1.06
CH_3	106-38-7	4.46	4.53	0.86	0.91
OCH_3	104-92-7	3.69	3.71	0.53	0.58
CHO	1122-91-4	2.98	3.00	0.11	0.14
CF_3	402-43-7	3.38	3.40		

Table IV[a]

p-XC_6H_4Br	p-XC_6H_4Br in CH_3OH, mol %								
	0.1	0.4	0.7	1	2	4	6	8	10
X = CH_3									
Yield, g	0.30	0.33	0.35	0.38	0.80	0.96	1.17	1.24	1.25
	0.34	0.34	0.38	0.28	0.95	0.91		1.20	1.21
Av yield, %	32	34	37	33	58	62	78	81	82
X = OCH_3									
Yield, g	0.21	0.31	0.38	0.38	0.88	1.00	1.13	1.09	1.08
	0.30	0.37	0.38	0.40	0.85	0.94	0.98	1.08	1.07
Av yield, %	25	34	38	39	58	65	70	72	72
X = H									
Yield, g	0.28	0.31	0.37	0.43	0.67	0.91	1.12	1.09	1.26
	0.36	0.36	0.38	0.41	0.77	0.94	1.06	1.15	1.25
Av yield, %	32	34	38	42	48	62	73	75	84
X = CF_3									
Yield, g	0.34	0.41	0.41	0.42	0.80	1.17	1.21	1.29	1.27
	0.28	0.38	0.40	0.46	0.77		1.11	1.26	1.26
Av yield, %	31	40	41	44	52	78	77	85	84
X = CHO									
Yield, g	0.33	0.35	0.35	0.39	0.79	0.89	1.25	1.16	1.30
	0.35	0.38	0.41	0.44	0.63	1.19		1.34	1.22
Av yield, %	34	37	38	42	47	69	83	83	84

[a] Eight blank samples were also photolyzed, four of which contained 1.0 g of 1 in methanol (total volume 10 mL) and four of which contained 1.5 g of 1 in methanol (total volume 15 mL). See Table I and the Experimental Section. The observed yields were 0.20 (20%), 0.18 (18%), 0.19 (19%), 0.21 (20%), 0.23 (15%), 0.35 (23%), 0.32 (21%), and 0.18 g (12%). These may be compared to a literature value of 42.5% reported by Cowan and Drisko for their standardized conditions.[1]

on the heavy atom. However, while it seems likely that solvent dielectric constants will differ significantly at ArBr concentration levels near 10 mol %, they will differ very little at ArBr concentration levels near 1 mol %. For example, the dielectric constants of methanol and bromobenzene are 32.63 and 5.40, respectively, at 25 °C.[11] On the assumption that the dielectric constant for a binary liquid can be approximated by (mol fraction of A)(dielectric constant of A) + (mol fraction of B)(dielectric constant of B), dielectric constants of 29.91, 32.35, and 32.60 can be computed for bromobenzene in methanol at the 10, 1, and 0.1 mol % concentration levels. For p-bromoanisole (D = 7.06 at 30 °C),[12] the corresponding computed D values are 30.07, 32.37, and 32.60. The fact that the relative syn/anti ratios in this study follow the same substituent trend at 10 mol % ArBr in methanol as at 0.1 mol % ArBr in methanol (where dielectric constants are nearly identical) indicates that solvent dielectric is not a serious controlling factor here.

We have, at this time, no information concerning possible light absorption by the heavy-atom solvents and subsequent energy transfer from them to acenaphthylene, nor have we assessed the possibility of direct reactions between acenaphthylene and the aryl bromides.

Experimental Section

General. Acenaphthylene and all of the substituted bromobenzenes used in this investigation were purchased from the Aldrich Chemical Co. and were designated as 99% pure. Acenaphthylene was recrystallized twice from 95% ethanol (mp 90–91 °C), and p-bromobenzaldehyde was recrystallized twice from 95% ethanol (mp 57–58 °C). Bromobenzene (bp 154–156 °C), p-bromotoluene (bp 183–185 °C), p-bromoanisole (bp 215–216 °C), and p-bromobenzotrifluoride (bp 154–155 °C) were distilled prior to use.

Ultraviolet spectra were recorded on a Cary-17 UV–vis–near-IR spectrophotometer. All melting points and boiling points recorded herein are uncorrected.

Reaction Mixtures. Acenaphthylene (2.50 g) was dissolved in each binary solvent and diluted volumetrically with that solvent to 25 mL. A 10-mL aliquot (for solvents 0.1–1 mol % in ArBr) or a 15-mL aliquot (for solvents 2–10 mol % in ArBr) was subsequently removed and transferred to a Pyrex tube (25 cm long × 12 mm wide × 1 mm thick). Each reaction mixture was then degassed by two freeze (liquid N_2)–pump–thaw cycles, and each reaction vessel was sealed under vacuum.

Irradiation Procedure. Irradiations were conducted with a 450-W, Ace-Hanovia 6515-34 quartz mercury-vapor lamp fitted with a uranium glass sleeve and immersed in a Vycor cooling well. The reaction vessels were placed in a merry-go-round apparatus and situated 7.5 cm from the light source. For each set of data, 45 reaction mixtures were irradiated, but they could not be irradiated all at once. They were divided into batches of 20 (0.1–1.0 mol % in ArBr; all substituents), 15 (2–10 mol % in ArBr; H, CH_3, and OCH_3 substituents), and 10 (2–10 mol % in ArBr; CHO and CF_3 substituents). The first batch was accompanied with two "blanks" (1 in pure methanol), and the remaining batches were accompanied with one blank sample each. Thus, for both sets of data, eight blank samples were irradiated. The irradiations were continued for 15 h at room temperature, during which time the acenaphthylene photodimers precipitated from solution. The temperature of the reaction mixtures was ~30 °C during photolysis.

Product Analysis. The photodimers were isolated by filtration and washed with methanol (10 mL) to remove any 1 that may have coprecipitated during the reaction. The weights of dimer and percent conversions to dimer are summarized in Table IV for two sets of reactions. The dimer mixtures were then thoroughly powdered and subjected to UV analysis.

Solubility Measurements. The syn or anti photodimer (0.50 g) was added to 25 mL of a given solvent, and the mixture was allowed to stand with shaking for 20 h at ~22–24 °C. The insoluble material was subsequently removed by filtration, and the filtrate was con-