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An Unusual Property of Benzyl Diphenylphosphinothiite in the Reactions with Various Electrophilic Reagents

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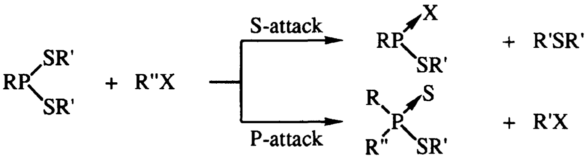
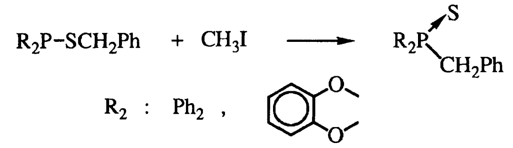
Reactions of benzyl diphenylphosphinothiite with a number of electrophiles have been investigated. It has been proved that a kinetically controlled process affords the S-attacked product, which is further converted into the transalkylated product, whereas a thermodynamically controlled process results in the formation of a P-attacked product. An intramolecular S → P migration of the benzyl group is suggested for the reactions with reactive electrophiles.

The reactions of P(III) thioesters have been investigated in detail. When the sulfur is attacked by an electrophile, a phosphonochloridothioite and the corresponding sulfide are formed,[1—3] whereas the classical Arbuzov reaction takes place when the phosphorus is the reaction center (Eq. 1).[4,5]



(1)

In our earlier communications, we reported the synthesis of a new class of phosphorus compounds, benzyl diphenylphosphinothiite, and 2-benzylthio-4,5-benzo-1,3,2,-dioxaphospholane.[6,7] It has also been found that they react with methyl iodide resulting in the formation of benzyldiphenylphosphine sulfide and a phosphonothioate, respectively.[8] In contrast to their oxygen analogs,[9] the initial attack of an electrophile takes place on the sulfur atom in these compounds that have the P–S bond (Eq. 2).[8]



(2)

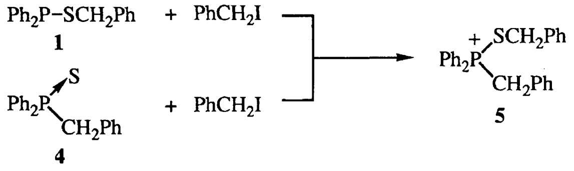
Since we have currently been interested in the properties of the >P–SCH$_2$Ph system, we have studied the reaction of benzyl diphenylphosphinothiite with a number of electrophiles in detail. The results from our investigation will be reported in the present paper.

Results and Discussion

When benzyl diphenylphosphinothiite (**1**) and methyl iodide were allowed to react inside the cavity of an NMR spectrometer at a temperature range between −20 to +20°C, a ^{31}P and a ^{1}H NMR signals appeared at δ_P=32.5 and δ_H=2.30 (d, 3H, $^3J_{HP}$=11.8 Hz), respectively. The ^{1}H NMR spectrum also exerted a signal at δ_H=4.52 which is assignable to the benzylic protons in benzyl iodide. The ^{31}P and ^{1}H NMR signals can be attributed to the formation of methyl diphenylphosphinothiite (**2**).[10] The increase in the temperature resulted in the disappearance of the initially appeared ^{31}P and ^{1}H signals and new signals appeared at δ_P=35.0 and δ_H=3.96 (d, 2H, $^2J_{HP}$=11.8 Hz) and 2.28 (d, 3H, $^3J_{HP}$=13.8 Hz). The newly appeared signals are attributable to the formation of benzyl(methylthio)diphenylphosphonium iodide (**3**), in which the benzyl group is attached to the phosphorus atom.

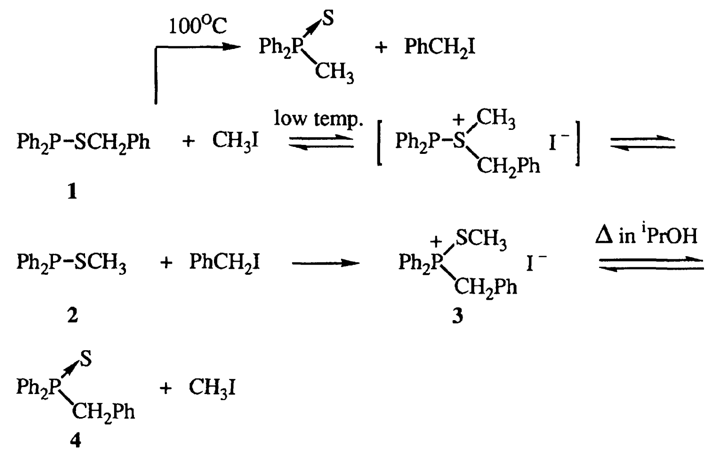
When the reaction was run at 100°C, the sole product obtained was methyldiphenylphosphine sulfide (δ_P= 35.5). Thus, it is found that the classical Arbuzov reaction is favored at higher temperatures. The reactions are summarized in Scheme 1.

The reactions of **1** with ethyl iodide and benzyl bromide both afford benzyldiphenylphosphine sulfide (**4**) exclusively. On the other hand, when benzyl iodide is employed as an electrophile, both **1** and **4** afford benzyl(benzylthio)diphenylphosphonium iodide (**5**), a stable phosphonium salt (δ_P=45.0), as shown in Eq. 3.



(3)

Thus, it has been clarified that the phosphonium salt and the phosphine sulfide are essentially in thermodynamic equilibrium; the benzyl group rather prefers to leave from the sulfur atom of the phosphonium salt when the counter ion is the bromide, whereas benzyl iodide attacks the sulfur atom of the phosphine sulfide to release an iodide anion.[11] It is known that an alkyl bromide requires more rigorous conditions than the corresponding iodide to react with phosphine sulfides.[12] It is interesting to note that ^{1}H NMR spectrum of **5** exerts two signals with an identical HP-coupling

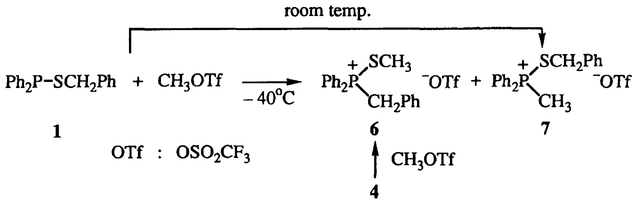


Scheme 1.

constant for two benzyl protons ($\delta_H = 4.42$ and 4.24, $^2J_{HP} = {}^3J_{HP} = 13.8$ Hz)

To extend the investigation further, **1** was allowed to react with more reactive electrophiles such as methyl trifluoromethanesulfonate (triflate), triethyloxonium tetrafluoroborate, and dimethyl sulfate.

Methyl triflate reacts with **1** at −40°C to afford two phosphonium salts that exert ^{31}P NMR signals at $\delta_P = 52.1$ and 44.6, respectively. The latter salt is the major product. Based on the comparison of ^{1}H and ^{31}P NMR spectra of the reaction mixture with those of benzyl(methylthio)diphenylphosphonium triflate (**6**), independently synthesized by the reaction of **4** with methyl triflate, the minor product is assigned to **6**, while the major product has been identified to be benzylthio(methyl)diphenylphosphonium triflate (**7**), in which the methyl group is attached to the phosphorus atom (Eq. 4).

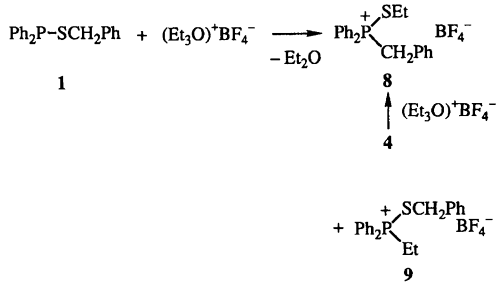


(4)

When **1** and methyl triflate are mixed at room temperature, an exothermic reaction takes place resulting in the formation of **7** ($\delta_P = 44.6$) as the sole product. Thus, here, increased reactivity of an electrophile results in the alkylation on the phosphorus atom predominantly. The decreased reaction temperature, however, favors the formation of an S-alkylated product. Thus, the P-alkylation is a thermodynamically controlled process, whereas the S-alkylation is a kinetically controlled process.

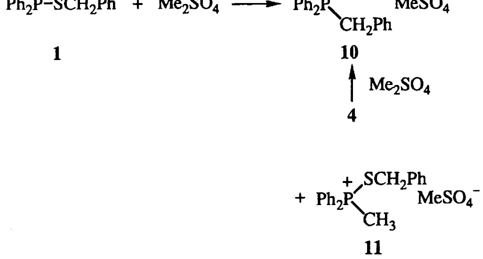
It is noteworthy that ^{1}H NMR spectra of **6** and **7** exert signals from their methyl and benzyl protons at different positions, respectively, while their HP-coupling constants are kept constant as was observed in the phosphonium salt **5**.

The reaction of **1** with triethyloxonium tetrafluoroborate at room temperature in dichloromethane also affords a mixture of two phosphonium salts in the ratio of 2 ($\delta_P = 47.8$) : 3 ($\delta_P = 51.0$), which is recognized by ^{31}P NMR signals. Since the reaction of **4** with triethyloxonium tetrafluoroborate affords benzyl(ethylthio)diphenylphosphonium tetrafluoroborate (**8**) with $\delta_P = 47.8$, it is concluded that the other phosphonium salt is benzylthio(ethyl)diphenylphosphonium tetrafluoroborate (**9**), the salt formed by the P-attack of the electrophile (Eq. 5).



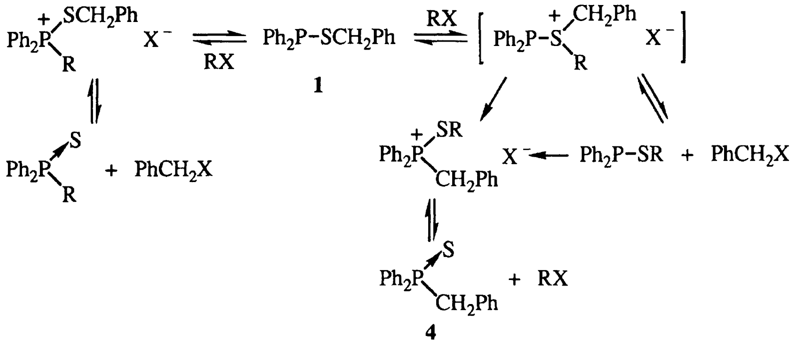
(5)

The reactions of **1** and **4** with dimethyl sulfate proceed similarly; the former affords a mixture of two phosphonium salts, benzyl(methylthio)diphenylphosphonium methylsulfate (**10**) and benzylthio(methyl)diphenylphosphonium methylsulfate (**11**), that resonate at $\delta_P = 43.0$ and 41.0, respectively (Eq. 6), and the latter affords **10** as the sole product.



(6)

In contrast to the other phosphonium salts, **5**, **6**, and



Scheme 2.

7, the $^2J_{HP}$-coupling constants in ^{1}H NMR spectra of **10** and **11** are smaller than the corresponding $^3J_{HP}$-coupling constants ($^2J_{HP}$=13.2 Hz vs. $^3J_{HP}$=13.4 Hz). However, the values for $^2J_{HP}$ and $^3J_{HP}$ are the same, respectively, regardless the protons are methylic or benzylic.

In conclusion, the reaction of **1** with an alkyl halide proceeds kinetically via an initial attack of the electrophile on the sulfur atom of the P–S diade resulting in the formation of a transalkylated phosphonium salt or a phosphine sulfide depending on the reaction conditions. However, at an elevated temperature, the thermodynamic control predominates and the attack of an electrophile on the phosphorus atom takes place resulting in the formation of a phosphine sulfide via the classical Arbuzov reaction.

The formation of the P-benzyl phosphonium salt, **6**, **8**, and **10** from the reaction of **1** with methyl triflate, triethyloxonium tetrafluoroborate, and dimethyl sulfate, respectively, could be attributed to the direct intramolecular S → P migration of the benzyl group instead of the intermolecular benzylation of methyl diphenylphosphinothiite by, for example, benzyl triflate once produced as an intermediate. There is no reason to expect the formation of unstable (then, reactive) benzyl triflate as the intermediate. An S-benzyl sulfur ylid is known to undergo similar migration of the benzyl group from the sulfonium sulfur to the carbanionic center.[13] Since benzyl triflate is so unstable, or so reactive, that the equilibrium is largely shifted toward the phosphonium side and the kinetically controlled transalkylated products, methyl diphenylphosphinothiite and benzyl triflate, are unable to be isolated under the conditions employed for the reaction of **1** with methyl triflate. Consequently, the product which can be isolated is the thermodynamically controlled one only. The formations of the other P-benzyl phosphonium salts, **8** and **10**, may also be accounted for by the intramolecular benzyl-migration. The whole scheme is summarized in Scheme 2.

Experimental

Instruments. ^{1}H NMR spectra were recorded on a Bruker WM-250 spectrometer at 250.13 MHz at a temperature range between −20 and +25°C in dichloromethane-d_2 with TMS as an external standard unless otherwise indicated. ^{31}P NMR spectra were recorded on a Bruker CXP-100 spectrometer at 36.47 MHz at a temperature range between −60 and +30°C in the same solvent. Boiling and melting points were not corrected.

Materials and General Procedure. Dichloromethane was purified by a standard procedure. Benzyl iodide was synthesized via the Finkelstein reaction from sodium iodide with benzyl chloride in acetone. Methyl trifluoromethanesulfonate[14] and triethyloxonium tetrafluoroborate[15] were prepared according to the literature procedures. All reactions were carried out with each 9 mmol of **1** and an electrophile under dry argon atmosphere in a dry glassware unless otherwise indicated.

Preparation of Benzyl Diphenylphosphinothiite (1). Chlorodiphenylphosphine (2 g, 9 mmol) and benzyl trimethylsilyl sulfide (1.78 g, 9 mmol) were mixed under argon atmosphere. After 12 h at room temperature, chlorotrimethylsilane was removed in vacuo leaving **1** as the sole product. Thus obtained **1** was used for the reactions without further purification. ^{31}P NMR δ_P=27.0.[6]

Reaction of 1 with Methyl Iodide. Equimolar amounts of **1** and methyl iodide were mixed at ambient temperature. After 1 h, the reaction mixture was worked-up to isolate yellow crystals of benzyl(methylthio)diphenylphosphonium iodide (**3**). ^{31}P NMR δ_P=35.0; ^{1}H NMR δ_H=2.28 (d, $^3J_{HP}$=13.8 Hz, 3H, SC**H$_3$**), 3.96 (d, $^2J_{HP}$=11.8 Hz, 2H, PhC**H$_2$**), 7.36—7.64 (m, 10H, **Ph**), and 7.80—7.99 (m, 5H, **Ph**CH$_2$).

Recrystallization of the crystals from isopropyl alcohol afforded benzyldiphenylphosphine sulfide (**4**) in 68% yield (2.44 g): Mp 162°C. ^{31}P NMR (DMF) δ_P=42.1; ^{1}H NMR (DMSO-d_6) δ_H=4.10 (d, 2H, $^2J_{HP}$=14.0 Hz, 2H, PC**H$_2$**Ph), 7.05 (s, 10H, P**Ph**), and 7.45 (m, 5H, **Ph**CH$_2$). Found: C, 73.97; H, 5.49; P, 10.01; S, 10.30%. Calcd for $C_{19}H_{17}PS$: C, 74.03; H, 5.52; P, 10.06; S, 10.39%.

Reaction of 1 with Methyl Iodide at a Higher Temperature. A mixture of **1** and methyl iodide was heated at 100°C for 15 min. Methyldiphenylphosphine sulfide was isolated by distillation in vacuo in 70% yield (1.46 g): Bp 158—160°C (2.7 Pa): n_D^{25} 1.6503.[16] ^{31}P NMR δ_P=35.5; ^{1}H NMR δ_H=3.10 (d, $^2J_{HP}$=13.5 Hz, 3H, PC**H$_3$**) and 7.31 (m, 10H, P**Ph**).

Reaction of 1 with Ethyl Iodide. Equivalent amounts of **1** and ethyl iodide were mixed as described above. After 24 h at room temperature, white crystals of **4**

were isolated in 75% yield (2.38 g): Mp 162°C. $^{31}\mathrm{P}$ NMR (DMF) $\delta_\mathrm{P}=42.1$

Reaction of 1 with Benzyl Bromide. The reaction of **1** with benzyl bromide afforded **4** in 75% yield (2.38 g) similarly as described above.

Reaction of 1 with Benzyl Iodide. Equivalent amounts of **1** and benzyl iodide were mixed at room temperature. After 1 h, the mixture became yellow. Within 1 more hour, brown crystals were obtained. The crystals were washed with pentane to give benzyl(benzylthio)diphenylphosphonium iodide (**5**) in 75% yield (3.50 g): Mp 137°C. $^{31}\mathrm{P}$ NMR $\delta_\mathrm{P}=45.0$; $^{1}\mathrm{H}$ NMR $\delta_\mathrm{H}=4.24$ (d, $^3J_\mathrm{HP}=13.8$ Hz, 2H, $\mathrm{SC\mathbf{H}_2Ph}$), 4.42 (d, $^2J_\mathrm{HP}=13.8$ Hz, 2H, $\mathrm{C\mathbf{H}_2Ph}$), 7.45 (m, 10H, $\mathrm{\mathbf{Ph}CH_2}$), and 7.81 (m, 10H, $\mathrm{P\mathbf{Ph}}$).

Reaction of 1 with Methyl Triflate. Methyl triflate was added to an equivalent amount of **1** at room temperature. After 2 h, a quantitative amount of benzylthio(methyl)diphenylphosphonium triflate (**7**) was obtained (4.28 g). No further purification was attempted: n_D^{23} 1.5692. $^{31}\mathrm{P}$ NMR $\delta_\mathrm{P}=44.6$; $^{1}\mathrm{H}$ NMR $\delta_\mathrm{H}=2.74$ (d, $^2J_\mathrm{HP}=13.8$ Hz, 3H, $\mathrm{PC\mathbf{H}_3}$), 4.13 (d, $^3J_\mathrm{HP}=11.8$ Hz, 2H, $\mathrm{SC\mathbf{H}_2Ph}$), 7.20 (s, 5H, $\mathrm{CH_2\mathbf{Ph}}$), and 7.70—7.82 (m, 10H, $\mathrm{P\mathbf{Ph}}$). Found: C, 53.31; H, 4.19; P, 6.49; S, 13.53%. Calcd for $\mathrm{C_{21}H_{20}O_3PS_2F_3}$: C, 53.39; H, 4.24; P, 6.57; S, 13.56%.

Reaction of Benzyldiphenylphosphine Sulfide (4) with Methyl Triflate. The compound **4** was prepared by our standard procedure.[6—8] A solution of **4** (1.54 g, 5mmol) in dichloromethane (5 ml) and methyl triflate (0.82 g, 5 mmol) were mixed at ambient temperature. After 1 h, the removal of the solvent remained benzyl(methylthio)diphenylphosphonium triflate (**6**) quantitatively (2.3 g): n_D^{20} 1.5687. $^{31}\mathrm{P}$ NMR $\delta_\mathrm{P}=52.1$; $^{1}\mathrm{H}$ NMR $\delta_\mathrm{H}=2.23$ (d, $^3J_\mathrm{HP}=13.8$ Hz, 3H, $\mathrm{SC\mathbf{H}_3}$), 4.55 (d, $^2J_\mathrm{HP}=11.8$ Hz, 2H, $\mathrm{C\mathbf{H}_2Ph}$), 7.16 (m, 5H, $\mathrm{PCH_2\mathbf{Ph}}$), and 7.60—7.76 (m, 10H, $\mathrm{P\mathbf{Ph}}$). Found: C, 53.32; H, 4.20; P, 6.492; S, 13.53%. Calcd for $\mathrm{C_{21}H_{20}O_3PS_2F_3}$: C, 53.39; H, 4.24; P, 6.57; S, 13.56%.

Reaction of 1 with Triethyloxonium Tetrafluoroborate. A solution of triethyloxonium tetrafluoroborate (1.71 g, 9 mmol) in 5 ml of dichloromethane was added to an equivalent amount of **1**. After 2.5 h at room temperature, the solvent was removed in vacuo leaving a mixture of **8** and **9**. $^{31}\mathrm{P}$ NMR $\delta_\mathrm{P}=47.8$ for **8** and 51.0 for **9**; $^{1}\mathrm{H}$ NMR $\delta_\mathrm{H}=1.25$ (t, 3H, $\mathrm{SCH_2C\mathbf{H}_3}$ in **8**), 1.51 (dt, $^3J_\mathrm{HP}=22.7$ Hz, 3H, $\mathrm{PCH_2C\mathbf{H}_3}$ in **9**), 2.75 (q, $^3J_\mathrm{HP}=10.7$ Hz, 2H, $\mathrm{SC\mathbf{H}_2CH_3}$ in **8**), 2.90 (dq, 2H, $\mathrm{PC\mathbf{H}_2CH_3}$ in **9**), 4.24 (d, $^3J_\mathrm{HP}=13.8$ Hz, 2H, $\mathrm{SC\mathbf{H}_2Ph}$ in **9**), 4.43 (d, $^2J_\mathrm{HP}=12.5$ Hz, 2H, $\mathrm{PC\mathbf{H}_2Ph}$ in **8**), 7.65—7.77 (m, 5H, $\mathrm{CH_2\mathbf{Ph}}$), and 7.78—7.90 (m, 10H, $\mathrm{p\mathbf{Ph}}$).

Reaction of 4 with Triethyloxonium Tetrafluoroborate. A solution of **4** (1.54 g, 5 mmol) in dichloromethane (5 ml) and triethyloxonium tetrafluoroborate (2.12 g, 5 mmol) in dichloromethane (5 ml) were mixed at room temperature. The solvent was removed in vacuo after 1.5 h and the residue was washed with pentane giving white needles of **8** in 95% yield (2.01 g): Mp 157°C. $^{31}\mathrm{P}$ NMR $\delta_\mathrm{P}=47.8$; $^{1}\mathrm{H}$ NMR $\delta_\mathrm{H}=1.25$ (t, 3H, $\mathrm{SCH_2C\mathbf{H}_3}$), 2.75 (q, $^3J_\mathrm{HP}=10.7$ Hz, 2H, $\mathrm{SC\mathbf{H}_2CH_3}$), 4.43 (d, $^2J_\mathrm{HP}=12.5$ Hz, 2H, $\mathrm{PC\mathbf{H}_2Ph}$), 7.65—7.77 (m, 5H, $\mathrm{CH_2\mathbf{Ph}}$), and 7.78—7.90 (m, 10H, $\mathrm{P\mathbf{Ph}}$). Found: C, 60.98; H, 5.28; P, 752; S, 7.70%. Calcd for $\mathrm{C_{21}H_{22}PSBF_4}$: C, 61.02; H, 5.33; P, 7.51; S, 7.75%.

Reaction of 1 with Dimethyl Sulfate. Equivalent amounts of **1** and dimethyl sulfate were mixed at room temperature. The reaction was found to be completed within 2 h and the reaction mixture became yellow. After usual work-up, a mixture of benzyl(methylthio)diphenylphosphonium methylsulfate (**10**) and benzylthio(methyl)diphenylphosphonium methylsulfate (**11**) was obtained in a quantitative yield. $^{31}\mathrm{P}$ NMR ($\mathrm{CD_2Cl_2}$) $\delta_\mathrm{P}=43.0$ for **10** and 41.0 for **11**; $^{1}\mathrm{H}$ NMR ($\mathrm{CD_2Cl_2}$) $\delta_\mathrm{H}=2.67$ (d, $^3J_\mathrm{HP}=13.4$ Hz, 3H, $\mathrm{SC\mathbf{H}_3}$ in **10**), 3.27 (d, $^2J_\mathrm{HP}=13.2$ Hz, 3H, $\mathrm{PCH_3}$ in **11**), 3.93 (s, 3H, $\mathrm{\mathbf{CH_3}SO_4^-}$), 4.31 (d, $^3J_\mathrm{HP}=13.4$ Hz, 2H, $\mathrm{SC\mathbf{H}_2CH_3}$ in **11**), 5.00 (d, $^2J_\mathrm{HP}=13.2$ Hz, 2H, $\mathrm{PC\mathbf{H}_2Ph}$ in **10**), 7.30—7.48 (m, 5H, $\mathrm{CH_2\mathbf{Ph}}$), and 8.05—8.19 (m, 10H, $\mathrm{P\mathbf{Ph}}$).

Reaction of 4 with Dimethyl Sulfate. A solution of **4** (1.54 g, 5 mmol) in dichloromethane (5 ml) and dimethyl sulfate (0.63 g, 5 mmol) were mixed at room temperature. After 2 h, the solvent was removed in vacuo and the residue was washed with pentane leaving white crystals of **10** in 98% yield (2.12 g): Mp 152°C. $^{31}\mathrm{P}$ NMR $\delta_\mathrm{P}=43.0$; $^{1}\mathrm{H}$ NMR $\delta_\mathrm{H}=2.67$ (d, $^3J_\mathrm{HP}=13.4$ Hz, 3H, $\mathrm{PSC\mathbf{H}_3}$), 3.93 (s, 3H, $\mathrm{\mathbf{CH_3}SO_4^-}$), 5.00 (d, $^2J_\mathrm{HP}=13.2$ Hz, 2H, $\mathrm{PC\mathbf{H}_2Ph}$), 7.30—7.48 (m, 5H, $\mathrm{CH_2\mathbf{Ph}}$), and 8.05—8.19 (m, 10H, $\mathrm{P\mathbf{Ph}}$). Found: C, 58.03; H, 5.27; P, 7.12; S, 14.74%. Calcd for $\mathrm{C_{21}H_{23}O_4PS_2}$: C, 60.29; H, 5.50; P, 7.42; S, 15.31%.

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