Effects of Structure on the Free Radical Reactions of Hydridophosphoranes with Dimethyl Sulfide

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Introduction

Phosphoranyl radicals,[1] $Z_4P^{\bullet}$, are most often formed by oxidative addition of a free radical to a three-coordinate phosphorus compound and typically give products by subsequent scission processes. Less commonly, intact phosphoranyl radicals are trapped in bimolecular reactions, e.g., with CCl_4,[2] 5,5-dimethyl-1-pyrroline 1-oxide,[3] *t*-BuNO,[4] and molecular oxygen.[5] Phosphoranyl radicals with phosphorus included in a bicyclic or spirocyclic ring system are typically generated from hydridophosphoranes, Z_4PH, and are sufficiently stable toward self-cleavage that they can be trapped in displacement reactions (S_H2) with alkyl disulfides.[6,7] This reaction is in fact a key step in the substitution reactions of the bicyclic hydridophosphorane **4** (Chart 1) with disulfides.[6] We previously showed that these are free radical chain processes and proposed that they most probably proceed via the reaction mechanism given by eqs 1−3.[6]

The reaction of hydridophosphorane **4** with a series of dialkyl disulfides was shown to be strongly sensitive to the steric size of the alkyl substituent.[6] In competition reactions, the rate constant for reaction of the phosphoranyl radical intermediate from **4** for the series R = Me, *s*-Bu, neopentyl, and *t*-Bu varied over a nearly 600-fold range, demonstrating a severe steric influence on that process. We suggested[6] that this is consistent with reversible formation of a sulfuranyl radical intermediate (**19**), followed by rate-determining sulfur−sulfur cleavage, or a concerted process with a transition state having a relatively high degree of phosphorus−sulfur bond formation (eq 2).

Table 1. Reactions of Hydridophosphoranes with Methyl Disulfide[a]

hydrido-phosphorane	% methylthio-hosphorane formed		% starting material consumed	reaction time, h	δ ^{31}P **10**−**18**
1	**10**	99	100	4	−22.1
2	**11**	98	100	0.75	−6.8
3	**12**	5	50	14	−19.0
4	**13**	98	100	1.5	−27.5
5	**14**	4	40	14	−2.4
6	**15**	5	47	14	−90[b]
7	**16**	0	100	14	*c*
8	**17**	29	44	14	−1.6
9	**18**	10	76	14	−10.3

[a] Yields by ^{31}P NMR by integration vs external $(MeO)_3PO$ samples. [b] Assignment to **15** uncertain. [c] No peak assignable to **16** detected.

$$RSSR \xrightarrow{h\nu} 2RS^{\bullet}$$

$$Z_4PH + RS^{\bullet} \longrightarrow Z_4P^{\bullet} + RSH \qquad (1)$$

$$Z_4P^{\bullet} + RSSR \longrightarrow Z_4PSR + RS^{\bullet} \qquad (2)$$

$$Z_4PH + RSSR \longrightarrow Z_4PSR + RSH \qquad (3)$$

$$Z_4P^{\bullet} + RSSR \rightleftharpoons \underset{\textbf{19}}{\text{R(Z}_4\text{P)S}^{\bullet}\text{—SR}} \qquad (4)$$

The reaction system represented by reactions 1−4 presents a special opportunity to examine, at least qualitatively, effects of structural change in the reactant radical ($Z_4P^{\bullet}$) on a free radical substitution process taking place at sulfur. We report here reactions initiated by ultraviolet radiation of argon-purged solutions of a series of the individual hydridophosphoranes **1**−**9** with MeSSMe, a disulfide that is relatively unhindered sterically. The overall reaction is seen to be not broadly applicable to hydridophosphoranes as is it is very sensitive to variations in structure including steric crowding about phosphorus, the apical or equatorial position of the P−H bond in Z_4PH, and, perhaps also, the electronic structure of the phosphoranyl radical intermediate, $Z_4P^{\bullet}$.

Results and Discussion

Conversions of hydridophosphoranes were followed quantitatively by ^{31}P NMR spectroscopy for up to 14 h. In Table 1 it can be seen that only hydridophosphoranes **1** and **2**, in addition to the previously studied **4**, give high yields of the corresponding methylthiophosphoranes **10**, **11**, and **13**. The reaction of **4** was restudied to ensure that **1**−**9** were examined under the same conditions. The

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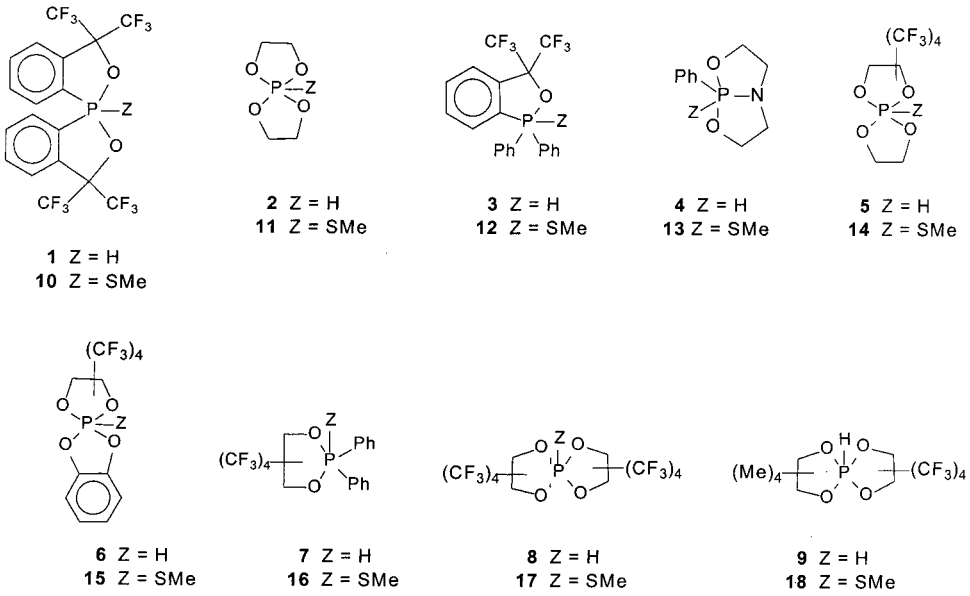
Chart 1



methylthiophosphorane is formed rapidly and essentially quantitatively from **1**, **2**, and **4**, as indicated by ^{31}P NMR analysis. Preparations of **10**, **11**, and **13**, carried out on a somewhat larger scale, gave near-quantitative amounts of product that was almost entirely pure (^{31}P NMR). Purification afforded **10**, **11**, and **13** in 84, 48, and 37% isolated yields, respectively. The phosphoranes were fully characterized spectroscopically and by quantitative elemental analysis.

The ^{31}P NMR chemical shifts of new phosphoranes **10** and **11** are upfield of external 85% H_3PO_4, as expected for molecules containing pentacoordinate phosphorus (Table 1). The ^{31}P chemical shifts of the trifluoromethyl-substituted compounds are less negative, as is well-known. The MeS functionalities of **10** and **11** reveal two-bond carbon−phosphorus couplings of 5.5 and 7.3 Hz, respectively. Their proton NMR spectra reveal three-bond Me−S couplings to phosphorus of 18−20 Hz. In addition to the phosphorus-coupled MeS peak, the ^{13}C spectrum of **11** shows only the expected doublet for the CH_2O functionality (J_{CP} = 2.0 Hz), while that for **10** also includes resonances that display appropriate fluorine couplings. CI mass spectra confirm the molecular masses for **10** and **11**.

By contrast, hydridophosphoranes **3** and **5**−**9** are only 40−50% consumed even over an extended 14-h irradiation time, with the exception of **7** which is totally consumed (Table 1). However, no evidence for methylthiophosphorane **16** formation from **7** is seen. The reactions of **3**, **5**, and **6** show peaks in their ^{31}P NMR spectra that perhaps are assignable to product methylthiophosphoranes (**12**, **14**, and **15**) but corresponding to only 4−5% yields. Reactions of hydridophosphoranes **8** and **9** show ^{31}P evidence for likely methylthiophosphorane formation (presumably, **17** and **18**) in marginally higher yields (29 and 10% respectively).

The results of Table 1 can be interpreted qualitatively, though somewhat speculatively, as follows. The very reactive hydridophosphoranes **1**, **2**, and **4** that give nearly quantitative yields of methylthiophosphorane have minimal steric congestion about phosphorus in the phosphoranyl radical intermediates that attack MeSSMe (eqs 2 and 4). The hydrogen abstracted in these pentacoordinate phosphorus reactants will be equatorial, and the odd electron/phantom ligand in the phosphoranyl radical should be pseudoequatorial,[1] as has been shown by ESR for the radical from **2**.[4]

Similarly, the phosphoranyl radical from the unreactive hydridophosphorane **3** lacks obvious steric congestion about phosphorus. However, **3** can be distinguished from **1**, **2**, and **4** in that its P−H bond is apical rather than equatorial (NMR and X-ray evidence).[8] If the odd electron in the corresponding phosphoranyl radical from **3** also is apical,[9] attack on sulfur in MeSSMe to introduce the MeS apically is likely disfavored by the weaker apical P−S bond formed and perhaps also *sterically* by the three adjacent equatorial substituents.

Spirophosphoranes **5**, **6**, **8**, and **9** that fail to readily undergo S−Me phosphorane formation possess equatorial P−H bonds and presumably generate phosphoranyl radicals with the odd electron pseudoequatorial. As noted earlier,[6] sulfuranyl radical intermediate **19** is potentially formed in reversible fashion prior to rate-determining generation of the methylthiophosphorane (eq 4). However, should sulfur−sulfur scission be very rapid, rate-determining irreversible sulfuranyl radical formation could be the key step. Alternatively, the attack of the phosphoranyl radical from hydridophosphorane **4** on RSSR may occur as a concerted displacement (eq 2). This displacement was strongly inhibited by sterically bulky R groups in RSSR, although alkylthiophosphoranes were still formed in high yields.[6] Analogously, the rate of reaction of a sterically hindered phosphoranyl radical with MeSSMe, by any of the three mechanisms (eq 2 or eq 4, reversible or irreversible) could be greatly reduced. Inspection of molecular models shows that Me and CF_3 substituents on the spiro rings of **5**, **6**, **8**, and **9** likely will destabilize intermediate **19** and affect eq 4 unfavorably. The transition state of a concerted S_H2 displacement on sulfur would be similarly destabilized sterically (eq 2). Both species are especially susceptible to 90° desta-

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(9) To our knowledge the ESR spectra of the phosphoranyl radicals from **3** and **7** have not been measured.

bilizing repulsions because of the T-shaped geometry about sulfur and linear P−S−S configuration.[10]

The marginally higher apparent yield of methylthiophosphorane from **8** compared to **9**, whose phosphoranyl radicals are similarly sterically hindered, seems at first surprising. However, CF_3 groups, being strongly electronegative, enhance the stabilities of five-coordinate phosphorus molecules[11] and may impart greater stability to the corresponding sulfuranyl intermediate or, alternatively, the transition state for a concerted displacement process.

Hydridophosphorane **5** is substituted on only one ring but still does not readily form the methylthiophosphorane. Significantly, **5** previously was reported to give the expected methylthiophosphorane (**14**, 80% yield by ^{31}P NMR) on UV light-initiated reaction with MeSSMe.[7] However, in that study the reactants were irradiated as a *neat solution with excess MeSSMe*, and the high concentration of MeSSMe would have increased the efficiency of trapping of the phosphoranyl radical. Apparently, the presence of eight CF_3 groups in **8** enhances the reactivity of the phosphoranyl radical intermediate sufficiently to overcome the effects of steric repulsions and lead to the marginally greater reactivity of **8** compared to **5**.

The presence of phenyl substituents on phosphorus in **1** clearly does not deter its reaction with MeSSMe. However, the structurally related hydridophosphoranes **6** and **7** fail to provide more than minimal yields of methylthiophosphorane. These reactions may be deterred sterically by the CF_3 substituents since **6** and **7** are tetrasubstituted as is the unreactive **5**. It can also be pointed out that the P−H bond of relatively unreactive hydridophosphorane **3** has been shown by X-ray crystallography to be apical[8] as is that for unreactive **7**.[12] Alternatively, the odd electron in the phosphoranyl radical from **3** and **7** may be delocalized into the π molecular orbital system as is known for certain other phenyl-substituted phosphoranyl radicals, sometimes referred to as π^* radicals.[1] This explanation seems less likely as hydridophosphorane **1** also is a phenyl phosphorane but nonetheless gives **10** essentially quantitatively. Furthermore, it should be noted that strongly electronegative substituents often destabilize the π^* form of a phosphoranyl radical in favor the more-usual s electronic structure.[1] Whether odd-electron apical or π^* phosphoranyl radicals that are not sterically impaired would participate readily in substitution reactions with alkyl disulfides is yet to be determined.

It is worth pointing out that the reaction of hydridophosphorane **6** with MeSSMe may be further inhibited by the intrinsic structure of **6**. Thus, the phosphorane form of **6** may in fact be in equilibrium with the ring-opened form having a phenolic moiety linked to three-coordinate phosphorus. Phenols are well-known inhibitors of free radical chain reactions. The electronegative nature of the CF_3 substituents, however, increases the stability of the pentacoordinate form[11] of **6** to minimize formation of ring-opened, phenolic material.

As can be noted in Table 1, the hydridophosphoranes that do not give high yields of methylthiophosphorane all are consumed to a significant extent over the typically 14-h irradiation period. Over a period of time MeSSMe, however, will continue to undergo photolysis to give free radicals. Even if the substitution at sulfur occurs inefficiently, the abstraction of hydrogen from the hydridophosphorane, reaction 1, is not likely to be very sensitive to hydridophosphorane structure and will lead slowly to its consumption. In fact the kinetic second-order consumption of phosphoranyl radicals has been reported.[1] Ultraviolet irradiation of a solution of **4** showed that it is not consumed without MeSSMe present.

Conclusions

Of the series of hydridophosphoranes **1**−**9**, only **1**, **2**, and the previously investigated **4** gave product methylthiophosphorane in very high yields. It is proposed that the reactions of certain of the phosphoranyl radical intermediates experience steric destabilization of the intermediate sulfuranyl radical or, if a concerted process is involved, on the transition state for attack at sulfur. This may be partially compensated for by electron-withdrawing, bond-strengthening trifluoromethyl groups. Variations in the position of the P−H bond and/or the electronic structures on the phosphoranyl radicals formed from **3**, **6**, and **7** evidently contribute to their failure to give product efficiently. Hydridophosphorane **6** may be self-inhibiting due to its potential free radical chain reaction with MeSSMe.

Experimental Section

General. Methyl sulfide (Aldrich) was distilled and stored over 4 Å molecular sieves. Hydridophosphorane **2** was prepared by the method of Wolf et al.[13] Hydridophosphoranes **1**[8] and **3**[8] were obtained from Professor J. C. Martin. Preparations of **4**,[14] **5**,[7] **6**,[15] **7**,[12] **8**,[16] and **9**[17] were previously reported. Benzene was distilled over calcium hydride and stored over 4 Å molecular sieves. Photolyses were carried out with a medium pressure 450-W Hanovia mercury lamp housed in a quartz cooling jacket. The reaction mixtures and the quartz cooling jacket were immersed in a water bath kept at room temperature. FT ^{31}P, ^{13}C, and ^{1}H NMR spectra were taken on Varian XL-100 and FT-80 spectrometers. The purities of the reaction products before workup were checked by ^{31}P NMR and GC. Quantitative elemental analyses were run by Galbraith Laboratories, Knoxville, TN. Mass spectra were obtained on a VG Micromass 7070-E double focusing, high-resolution mass spectrometer with a VG 2000 data system. Melting points are uncorrected.

Survey of Potential Photoreactions. Hydridophosphoranes **1**−**9** and methyl disulfide (0.03 to 0.2 mmol of each) were dissolved in C_6D_6 (0.50 mL) in 5 mm Pyrex NMR tubes. Argon was bubbled through each solution for 5 min, and the NMR tube was sealed with a cap. The cap was covered with Parafilm, and

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the tube was strapped to the cooling jacket of the photolysis apparatus. The reaction solutions were examined periodically by ^{31}P NMR. Phosphoranes **1**, **2**, and **4** were totally consumed in less than 4 h and showed only a peak assignable to the methylthiophosphorane. Percentages of the methylthiophosphoranes formed, and in the case of **3**, **5**, **6**, **8** and **9** of unreacted hydridophosphorane, were determined by reference to a capillary containing $(MeO)_3PO$ in the NMR tube. Ratios of ^{31}P signals were determined by ^1H-coupled ^{31}P NMR in C_6D_6 solvent.

Preparation of Methylthiophosphorane 10. Hydridophosphorane **1** (0.200 g, 0.356 mmol), methyl disulfide (0.0335 g, 0.356 mmol), and benzene (4.0 mL) were mixed in a 10 mL Pyrex tube. Argon was bubbled through the solution for 5 min. The tube was sealed with a rubber stopper. The cap was covered with Parafilm to ensure a good seal, and the sample was placed in the photolysis apparatus and irradiated for 4 h. The solvent was removed by freeze-drying to give the crude product **10** as a white solid which was purified by sublimation (oil bath temperature 50 °C, 0.05 mmHg) to give GLC-pure material (0.189 g, 0.306 mmol, 84% yield); mp 102−103 °C. ^{31}P NMR (32 MHz, C_6D_6) $\delta = -22.1$. ^1H NMR (C_6D_6, 100 MHz) δ 2.05 (d, $J_{HP} = 20.1$ Hz, 3 H, SCH_3), 7.05−7.45 (m, 4 H, $C_{12}H_8$), 7.55−7.80 (bm, 2 H, $C_{12}H_8$), 8.55−8.80 (M 2 H, $C_{12}H_8$). ^{13}C NMR (25 MHz, $CDCl_3$) δ 15.62 (d, $J_{CP} = 5.5$ Hz, SCH_3), 82.34 (m, $^2J_{CF} = 31.0$ Hz, *C*-CF_3), 122.70 (q, $^1J_{CF} = 289.6$ Hz, CF_3), 125.19 (d, $J_{CP} = 16.4$ Hz, aromatic), 132.00 (d, $J_{CP} = 14.7$, aromatic), 134.38 (bs, aromatic), 136.60 (d, $J_{CP} = 9.23$, aromatic). (Two of the six aromatic resonances are not seen or are overlapped with other peaks.) MS (CI isobutane) 563 (M + 1, 8.6), 517 (M − MeS, 100). Anal. Calcd for $C_{19}H_{11}F_{12}O_2PS$: C, 40.57; H, 1.96; P, 3.74. Found: C, 40.70; H, 2.09; P, 3.66.

Preparation of Methylthiophosphorane 11. Hydridophosphorane **2** (2.10 g, 13.8 mmol), methyl disulfide (1.30 g, 13.8 mmol), and benzene (20 mL) were mixed in a quartz tube and fitted with a rubber septum. Argon was bubbled through the solution for 5 min. The reaction mixture was irradiated for 45 min. The solvent was removed under reduced pressure to leave a sharply melting solid in essentially quantitative yield that showed a single peak in its ^{31}P NMR spectrum. This solid was Kugelrohr distilled to give an oily product which on standing at 0 °C crystallized to give GLC-pure material (1.30 g, 6.57 mmol, 48%): mp 56 °C. ^{31}P NMR (32 MHz, C_6D_6) $\delta = -6.8$ MHz. Anal. Calcd for $C_5H_{11}O_4PS$: C, 30.31; H, 5.60. Found: C, 30.09; H, 5.84. ^1H NMR (100 MHz, $CDCl_3$) δ 2.17 (d, 3H, $J_{HP} = 18$ Hz, SCH_3), 3.97 (d, 8H, $J_{HP} = 12$ Hz, CH_2). ^{13}C NMR (25 MHz, $CDCl_3$) δ 15.52 (d, $J_{CP} = 7.3$ Hz, SCH_3), 61.25 (d, $J_{CP} = 2.0$ Hz, OCH_2). MS (CI, isobutane) 199 (M + 1, 100), 151 (M − SCH_3, 88).

Preparation of Methylthiophosphorane 13. By the above procedure an argon-purged solution of **4** (1.30 g, 6.02 mmol) and dimethyl sulfide (0.58 g, 6.2 mmol) were dissolved in 20 mL of dry benzene. After deoxygenation with dry nitrogen, the solution was irradiated through Pyrex for 1 h. Benzene was removed by rotary evaporation to give a solid residue in virtually quantitative amounts that showed a single ^{31}P NMR peak corresponding to that of **13**. Kugelrohr distillation at less than 1 mmHg gave a colorless oil which turned solid on standing in a refrigerator: yield 0.590 g, 2.30 mmol, 38%, mp 46 °C. NMR spectra and mass spectra were in accord with that given previously in the literature.[6]

Control Irradiation of 4. Phosphorane **4** (2.37 g, 11.2 mmol) in 40 mL of argon-purged benzene was irradiated for 4 h, followed by removal of benzene under vacuum. Starting material was quantitatively reclaimed and showed a single ^{31}P NMR resonance assigned to **4**.

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