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A NEW PHOSPHINE-SULFIDES-TO-PHOSPHINE-OXIDES EXCHANGE REACTION

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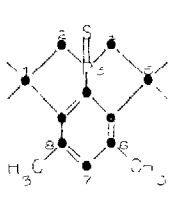
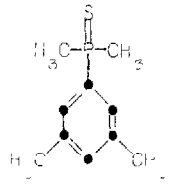
Summary: An unusual phosphine sulfide to phosphine oxide exchange reaction was found during the study of the annulation of (3,5-dimethylphenyl)-(2-hydroxy-2-methylpropyl)methylphosphine sulfide (3) using the mild cyclodehydration reagent methanesulfonic acid/phosphorus pentoxide.

In our work on the synthesis of the highly strained C-P heterocycle 1,1,5,5,6,8-hexamethylphospholano[3,2,1-hi]phosphindoline sulfide (1)[2] from 3,5-dimethylphenylphosphine sulfide (2),[3] we found an interesting phosphine sulfide to phosphine oxide exchange reaction which apparently is unprecedented.



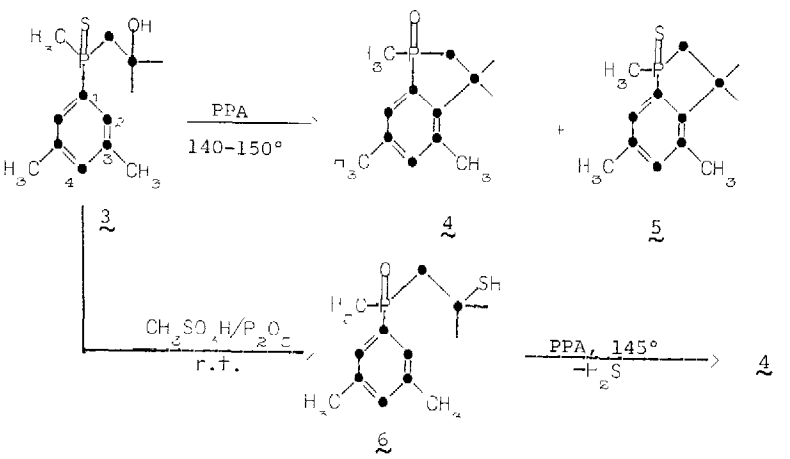
1



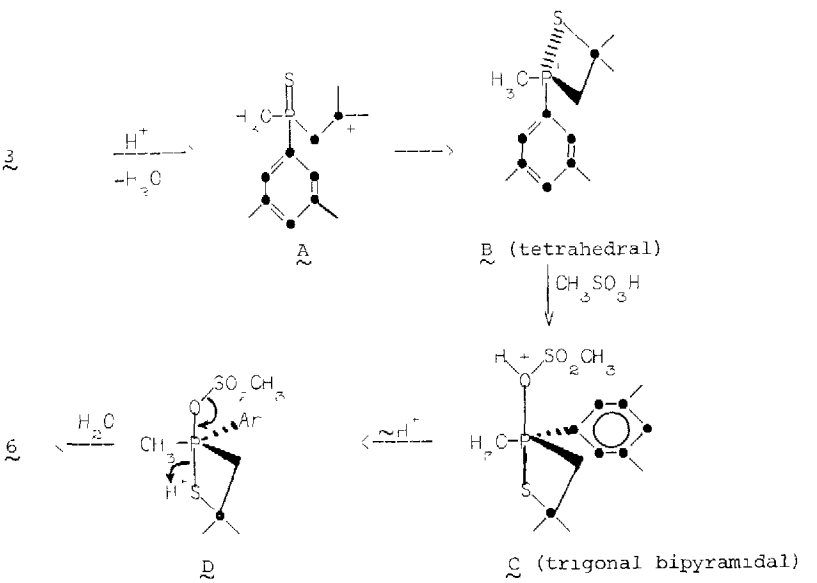
2

Lithiation of 2 followed by the addition of acetone produced 3,5-dimethylphenyl(2-hydroxy-2-methylpropyl)methylphosphine sulfide (3) in 47% yield. Polyphosphoric acid (PPA) treatment of the latter at 140-150° for 4 h unexpectedly gave mostly 1,3,3,4,6-pentamethylphosphindoline oxide (4) and a relatively small amount of the desired phosphine sulfide 5[3] in a ratio of ca. 3:1 (^{1}H NMR assey) These results suggest that under the strenuous reaction conditions of annulation, the P=S bond is also attacked by the reagent. In seeking milder reaction conditions for the annulation of 3, we used methanesulfonic acid/P_2O_5 at ambient temperature, following a literature procedure.[4] We isolated in 72% yield an isomer to which we assigned the structure (3,5-dimethylphenyl)-(2-mercapto-2-methylpropyl)methylphosphine oxide (6), based on its characteristic IR absorptions at 1170 (P=O) and 2510 (SH) cm^{-1} and its ^{1}H and ^{13}C NMR spectra.[3] The high-resolution mass spectrum of 6 showed a molecular ion m/e (%) at 256.1048 (11%) (M^+ for $C_{13}H_{21}OSP$ = 256.1050) and 167.0618 (100%) ($M^+ - C_4H_9S$), and the isomeric starting material 3 had m/e (%) at 256.1051 (37%) M^+ and a major fragment of 183.0000 (100%) for ($M^+-C_4H_9O$). The formation of 4 from the PPA annulation of 3 presumably resulted mostly from the mercaptan 6 formed *in situ* prior to ring closure. This is supported by the reaction of 6 with PPA under identical

conditions, in which the immediate evolution of H_2S was detected and 4 was isolated in 70% yield.



The mechanism of the sulfur-oxygen exchange reaction on the quaternary phosphorus in the isomerization of alcohol 3 to mercaptan 6 apparently involves the carbonium ion A formed by dehydration of 3 under acidic conditions. A is presumably short-lived, as it is quickly captured intramolecularly by the neighboring phosphine sulfide to form the quasi-phosphonium thiaphosphetane[5] B, which is inactive for annulation. The strained four-membered thiaphosphetanium ion B with tetrahedral phosphorus is expected to react rapidly with the solvent methanesulfonic acid, to release the ring strain upon passing from the tetrahedral to the trigonal bipyramidal structure C, in which the four-membered ring spans an apical-equatorial orientation.[6] Although the composition of the



reagent, methanesulfonic acid/phosphorus pentoxide, is not known, it was reported[4] that the solubility of P_2O_5 in methanesulfonic acid at room temperature is about 10%. The normal apical-apical displacement[7] in D should follow, after proton transfer, to give 6 upon aqueous workup.

This unusual sulfur-oxygen exchange reaction is interesting because the synthesis of phosphine oxides from the corresponding sulfides generally involves strong oxidizing agents, such as $KMnO_4$, HNO_3, Br_2 in alkaline solution, hydrogen peroxide, or thionyl chloride.[8] These reactions have certain disadvantages. For instance, alkyl side chains on aryl groups of tertiary phosphine sulfides were often oxidized to the carboxylic acids by potassium permanganate in pyridine.[9] Nitric acid also nitrated triphenylphosphine sulfide to tris-(m-nitrophenyl)phosphine oxide.[9] With excess thionyl chloride, tertiary phosphine sulfides gave dichlorophosphoranes.[10]

Thus, PPA and methanesulfonic acid/P_2O_5 reactions offer certain advantages in the conversion of phosphine sulfides to the corresponding oxides if nonoxidative and mild reaction conditions are to be met. This is exemplified by the conversion of 2 and triphenylphosphine sulfide to the corresponding phosphine oxides in yields of 65% and 63% by heating at 60°/24 h and 100°/48 h respectively with methanesulfonic acid/P_2O_5. Although PPA was also effective in these cases, yields were lower than in the methanesulfonic acid/P_2O_5 reactions, presumably due to the lower solubility of these compounds in PPA and the higher reaction temperature (140-150°) needed for reaction.

Both the acyclic triphenylphosphine sulfide and 2 require considerable heat and longer reaction times to complete the sulfur-oxygen exchange reaction. This may be attributed, in part, to the lack of relief of ring strain in these acyclic systems upon passing from the tetrahedral to the trigonal bipyramidal intermediates before displacement.[7]

References and Notes

1. Kodak Summer Research Fellow, 1978.
2. Named after the nitrogen analog, 1,2,4,5-tetrahydropyrrolo[3,2,1-hi]indole [F. A. L. Anet, J. M. Muchowski and E. Nishizawa, Chem. Ind. (London) 1117 (1961); H. Rapapport and J. R. Tretler, J. Am. Chem. Soc. 80, 5574 (1958)].
3. All new compounds gave satisfactory combustion analyses within ±0.4%. 2: Prepared from 3,5-dimethylbromobenzene by treating the corresponding Grignard reagent with dimethylthiophosphoryl bromide in 61% yield: m.p. 95.1°; ^{1}H NMR ($CDCl_3$) δ1.9 (d, 6H, J = 13 Hz), 2.35 (s, 6H), 7.1 (s, 1H), 7.4 (d, 2H, J = 14 Hz). 3: M.p. 74-75° (heptane); IR (KBr) 3450 (OH) (sharp) and 900 (P=S) (broad) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ1.2 (s, 3H, $-CH_3$), 1.4 (d, 3H, CH_3), 1.95 (d, 3H, J_{PCH} = 13 Hz, $-P(=S)CH_3$), 2.35 (s, 6H, $2ArCH_3$), 2.4 (d, 2H, $-P(=S)CH_2-$), 4.8 (s, 1H, -OH, deuterium exchangeable), 7.1 (s, 1H, p-ArH), 7.4 (d, 2H, J_{PCCH} = 14 Hz, o-ArH). ^{13}C NMR ($CDCl_3$) ppm rel. TMS δ23.8 (J_{PC} = 56.6 Hz, $-PCH_3$), 44.9 (J_{PC} = 53.7 Hz, $-PCH_3-$), 21.3

($ArCH_3$), 30.6, 31.2, 31.6, 32.2 (nonequiv. methyls), 70.8 (J_{PCC} = 3.9 Hz, methine OH), 132.6 (J_{PC} = 77.2 Hz, C-1 Ar), 127.6 (J_{PCC} = 10.7 Hz, C-2 Ar), 138.2 (J_{PCCC} = 12.7 Hz, C-3 Ar) and 133.0 (J_{PCCCC} = 2.9 Hz, C-4 Ar). 4: B.p. 136-138°/0.15 mm (solidified at r.t.; hygroscopic); HRMS m/e 222.1170 (M^+) (calc. for $C_{13}H_{19}OP$ = 222.1172). ^1H NMR ($CDCl_3$) δ1.5 (s, 3H, C-3 methyl), 1.6 (s, 3H, C-3 methyl), 1.7 (d, J_{PH} = 13 Hz, 3H, $-PCH_3$), 2.2 (m, 2H, $-PCH_AH_B-$), 2.35 (s, 3H, $ArCH_3$), 2.35 (s, 3H, $ArCH_3$), 2.5 (s, 3H, $ArCH_3$), 7.1 (s, 1H, p-ArH), 7.3 (d, J_{PH} = 12 Hz, 1H, o-ArH). 5: M.p. 125.5-127° (heptane); HRMS m/e 238.0934 (calc. for $C_{13}H_{19}PS$ = 238.0944). ^1H NMR ($CDCl_3$) δ1.5 (s, 3H, C-3 methyl), 1.6 (s, 3H, C-3 methyl), 1.95 (d, J_{PH} = 13 Hz, 3H, $-PCH_3$), 2.33 (s, 3H, $ArCH_3$), 2.43 (s, 3H, $ArCH_3$), 2.44 (m, partially buried, 2H, $-PCH_AH_B-$), 7.1 (s, 1H, p-ArH), 7.3 (d, J_{PH} = 12 Hz, 2H, o-ArH). 6: ^1H NMR ($CDCl_3$) δ1.5 (s, 3H, $-CH_3$), 1.6 (s, 3H, $-CH_3$), 1.7 (d, 3H, J = 12 Hz, $-P(=O)CH_3$), 2.35 (s, 6H, $2ArCH_3$), 2.45 (d, 2H, $-P(=O)CH_2-$), 2.8 (s, 1H, -SH, deuterium exchangeable), 7.1 (s, 1H, p-ArH), 7.3 (d, 2H, J = 12 Hz, o-ArH). ^{13}C NMR ($CDCl_3$) ppm rel. TMS δ19.2 (J_{PC} = 70.3 Hz, $-PCH_3$), 21.2 ($ArCH_3$), 33.8, 34.1, 34.3, 34.8 (nonequiv. methyls), 48 (J_{PC} = 66.4 Hz, $-PCH_2-$), 42.8 (J_{PCC} = 4.9 Hz, methine SH), 134.6 (J_{PC} = 95.7 Hz, C-1 Ar), 127.2 (J_{PCC} = 8.8 Hz, C-2 Ar), 138 (J_{PCCC} = 11.7 Hz, C-3 Ar), 132.9 (J_{PCCCC} = 2.9 Hz, C-4 Ar). 3,5-Dimethylphenylphosphine Oxide: Extremely hygroscopic; HRMS m/e 182.0836 (M^+) (calc. for $C_{10}H_{15}OP$ = 182.0859). ^1H NMR ($CDCl_3$) 1.7 (d, J = 12 Hz, 6H, $-PCH_3$), 2.35 (s, 6H, $2ArCH_3$), 7.2 (s, 1H, p-ArH), 7.4 (s, 2H, 2 o-ArH).

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