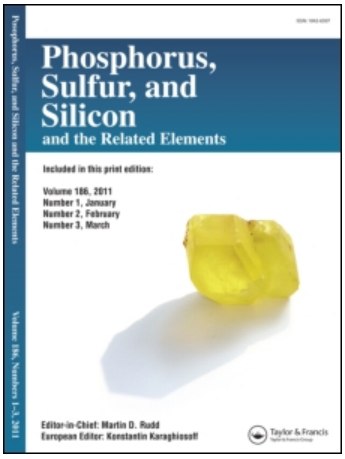

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CARBON-PHOSPHORUS HETEROCYCLES. REACTIONS OF THE ENAMINE 1-(1,2,3,6-TETRAHYDRO-1-PHENYL-4-PHOSPHORINYL) PYRROLIDINE *P*-SULFIDE WITH ACTIVATED ALKENES AND ACID ANHYDRIDES

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CARBON–PHOSPHORUS HETEROCYCLES. REACTIONS OF THE ENAMINE 1-(1,2,3,6-TETRAHYDRO-1-PHENYL-4-PHOSPHORINYL) PYRROLIDINE *P*-SULFIDE WITH ACTIVATED ALKENES AND ACID ANHYDRIDES

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The enamine of 1-phenyl-4-phosphorinanone 1-sulfide has been prepared for the first time from the ketone and pyrrolidine in benzene. Crude enamine could be cyanoethylated at carbon. Hydrolysis of the product followed by treatment of the nitrile with aqueous KOH gave the corresponding carboxylic acid. Reduction of this keto acid with $NaBH_4$ in alkaline medium gave the expected carbinol which lactonized spontaneously. Independent synthesis of the keto acid was achieved by adding methyl acrylate to the crude enamine followed by hydrolysis.

The crude enamine also reacted with methyl vinyl ketone in dry benzene. Surprisingly, the product was a bicyclic unsaturated ketone which apparently formed via an aldol type condensation (intramolecular) during the hydrolysis of the enamine reaction mixture (hydrolysis was effected with $H_2O/CH_3CO_2H/NaO_2CCH_3$). Interestingly, the crude enamine did *not* react with mesityl oxide or 1-acetyl-1-cyclohexene as only starting material and a polymeric substance could be obtained. Freshly distilled acetic anhydride or propionic anhydride did react with the crude enamine to give a solid product in each instance in modest yields. NMR analysis indicated a high population of the enol form in each example. Reaction of the acetyl derivative with hydrazine gave a phosphorinopyrazole and with hydroxylamine a mixture of phosphorinoisoxazoles. These are the first members of these heterocyclic families to be reported. Characterization via ^1H, ^{13}C and ^{31}P NMR analysis is also recorded for all compounds.

INTRODUCTION

Stork and co-workers[1a] demonstrated the ability of enamines to undergo attack by electrophilic alkenes and acid anhydrides and to give only C-alkylated or C-acylated products(s).[1] Little work has been done on enamines of phosphorinanones. Only one paper has been recorded in the literature by Märkl and co-workers on an enamine of 4-phosphorinanone in a reaction with a pyrylium salt, benzonitrile oxide or diphenylnitrilimine to give cycloaddition adducts.[2] Because of active interest[3] in functionalized phosphorus heterocycles, we now reveal our results on studies of the enamine of 1-phenyl-4-phosphorinanone 1-sulfide. Also we report herein the synthesis of several new bicyclic, phosphorus-containing heterocycles.

RESULTS AND DISCUSSION

1-(1,2,3,6-Tetrahydro-1-phenyl-4-phosphorinyl)pyrrolidine *P*-sulfide (**1**) was prepared by the treatment of 1-phenyl-4-phosphorinanone 1-sulfide (**2**)[4] with pyr-

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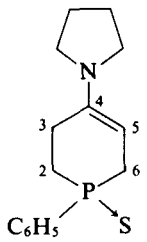
rolidine in benzene and with a catalytic amount of *p*-toluenesulfonic acid (PTSA) added. The mixture was boiled for 18–28 h under N_2 using a Dean–Stark apparatus to remove water. Although the enamine distilled as a heavy yellow oil at 190–195°C/0.025 mm, it decomposed on exposure to the atmosphere or upon standing. Therefore, essentially crude enamine was used in all further reactions.



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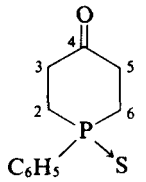
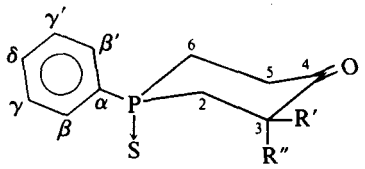


2

Enamine **1** was allowed to react with freshly distilled acrylonitrile in dry benzene. Normal hydrolysis and workup of the reaction mixture yielded only starting ketone **2**. When the reaction mixture was heated for 70–80 h, only polymeric material was obtained after hydrolysis. However, when the reaction mixture was boiled in absolute C_2H_5OH for 30–40 h, only a mono C-alkylated product could be isolated by column chromatography and was characterized as 4-oxo-1-phenyl-3-phosphorinanepropionitrile 1-sulfide (**3a**). The material displayed a single spot with TLC. IR analysis showed a carbonyl band (1710 cm^{-1}) and a nitrile band (2250 cm^{-1}). Interestingly, ^{31}P NMR absorption occurred as a sharp singlet at +33.13 ppm (relative to 85% H_3PO_4) and suggested the presence of only one isomer, likely **3a**. Formation of the axial β-cyanoethyl-substituted phosphorinanone **3b** is probably not favorable because of 1,3-diaxial interactions with the axial P → S bond and H(5a). ^1H NMR (100 MHz) analysis of **3a** was difficult since all of the ring protons and side chain protons appeared as a broad, complex multiplet in the range of δ 1.50–3.75. In con-



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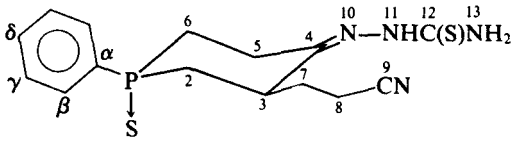


4

a. R′ = $\overset{7}{CH_2}$—$\overset{8}{CH_2}$—$\overset{9}{CN}$; R″ = H

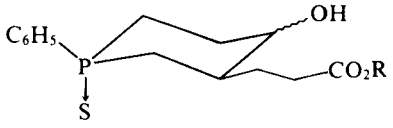
b. R′ = H; R″ = CH_2CH_2CN

c. R′ = CH_2—CH_2—CO_2H; R″ = H

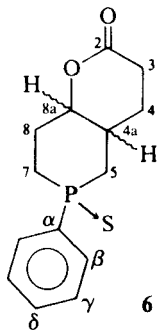
trast, the ^{13}C NMR spectrum was quite informative (see Experimental). In addition to the expected ^{13}C resonances, signals for the carbons alpha [C(2) and C(6)] to the P → S group appeared at 37.43 ppm ($^1J_{PC}$ = 49.83 Hz) and 31.84 ppm ($^1J_{PC}$ = 52.09 Hz). The chemical shift for C(2) is quite downfield in comparison to that in simple phosphorinanone **2**.[4] The shift for C(2) in **3a** is attributed to a β-deshielding effect by the substituent[5] at C(3). The downfield shift of C(3) in comparison with C(5) is due to the cyanoethyl substituent at C(3) (see Table II).[5c] The chemical shift of the cyanide carbon C(9) was observed at 118.88 ppm and was reasonable.[6]

The thiosemicarbazone derivative **4** was prepared and gave a lone ^{31}P NMR signal at +29.24 ppm (relative to 85% H_3PO_4). Derivative **4** was insoluble in most of the organic solvents but the ^1H NMR and ^{13}C NMR spectra were obtained in DMSO-d_6. The ^1H NMR spectrum of **4** was very complex and not significantly informative. Moreover, due to severe overlap of ^{13}C NMR signals with those from DMSO-d_6, it was not possible to assign upfield carbon signals. The sulfur-bearing carbon gave a signal at 179.14 ppm that of the C=N group at 152.73 ppm ($^3J_{PC}$ = 4.55 Hz).

Keto nitrile **3a** was hydrolyzed in boiling aqueous KOH solution under N_2 for 36 h, and subsequent acidification gave 4-oxo-1-phenyl-3-phosphorinanepropionic acid 1-sulfide (**3c**). Keto acid **3c** gave only one ^{31}P NMR signal at +27.95 ppm, supportive of one isomer with probably the C(3)-$CH_2CH_2CO_2H$ bond being equatorial. The ^1H NMR spectrum (100 MHz) of **3c** was very complex due to severe signal



5 a. R = Na
b. R = H



6

7

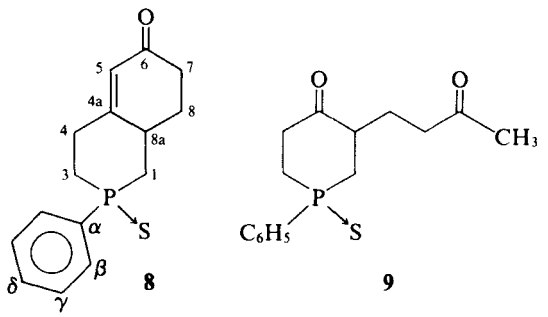
overlap. ^{13}C NMR analysis of **3c** (in DMSO-d_6) was difficult since most of the ring carbons gave signals that overlapped with those of in DMSO-d_6. Of course, carbonyl carbon C(4) and carboxylate carbon C(9) had resonances at 207.44 ppm [$^3J_{PC}$ = 5.29 Hz] and 174.26 ppm, respectively.[7] IR analysis of **3c** showed C=O absorption of a carbonyl and a carboxylate groups at 1697 cm^{-1} and 1712 cm^{-1}, respectively, and an O—H band at 3338 cm^{-1}.

Acid **3c** dissolved in an alkaline solution was reduced by $NaBH_4$ to carbinol **5a** at room temperature. The mixture was acidified (pH = 1–2) carefully with concentrated HCl. Lactonization occurred spontaneously and **6** was obtained after workup along with some hydroxy acid **5b** as identified by IR analysis. The crude material was taken up in benzene, and, after a few crystals of PTSA were added, the resulting mixture was boiled with a Dean Stark apparatus to lactonize the hydroxy acid. Again only one isomer was suggested by a lone ^{31}P NMR signal at +33.75 ppm (relative to 85% H_3PO_4). In addition to the expected ^{13}C resonances signals for the aliphatic carbons alpha [C(5) and C(7)] to the P → S group appeared at 35.96 ppm ($^1J_{PC}$ = 50.70 Hz) and 29.41 ppm ($^1J_{PC}$ = 44.03). We tentatively suggest that the former resonance is for C(5) which is alpha to C(4a). Similarly, based on the $^2J_{PC}$ couplings, the ^{13}C NMR signals were assigned for C(4a) and C(8) at 28.09 ppm [$^2J_{PC}$ = 6.02 Hz] and 27.28 ppm [$^2J_{PC}$ = 5.19 Hz], respectively. The resonance for carbon C(8a) appeared at 82.30 ppm [$^3J_{PC}$ = 3.63 Hz], which was quite reasonable for a carbon attached directly to oxygen.[9] Also, C(2) had a peak at 169.48 ppm, a typical shift for carbonyl carbon[7,9] of a δ-lactone. The four-bond coupling to C(3) was somewhat unexpected ($^4J_{PC}$ = 3.10 Hz) for the signal which appeared at 33.32 ppm.

The ^1H NMR spectrum of **6** was very complex, but signals for H(8a) could be

identified at δ 3.85–4.40.[10] The stereochemistry of the ring junction could not be inferred from the spectral data, however.

Keto acid **3c** was also obtained via treatment of enamine **1** with methyl acrylate followed by hydrolysis.[1] Two major spots were detected by TLC analysis of the reaction mixture, and the components were separated via column chromatography. Upon elution with C_6H_6:$HCCl_3$ (1:1), the ester **7** (48.2%) was obtained. Elution was continued with $HCCl_3$:CH_3OH (20:1) and gave the keto acid **3c** (11.2%). All properties of this product were identical to those of the keto acid **3c** obtained via hydrolysis of the keto nitrile **3a.** Although ester **7** showed bands for C=O of the keto (1706 cm^{-1}) group and ^1H NMR analysis of **7** revealed a singlet for CH_3 at δ 3.64, ^{31}P NMR analysis showed five signals at +33.57, +33.02, +32.15, +31.54 and +29.54 ppm (relative to 85% H_3PO_4). Thus **7** was apparently not pure, and the crude material was hydrolyzed with base to give, after neutralization, an acidic product which has resisted all attempts at purification.



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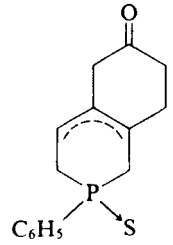

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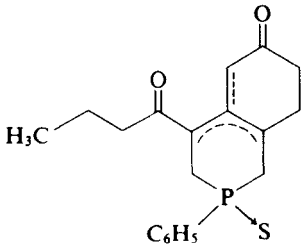


11

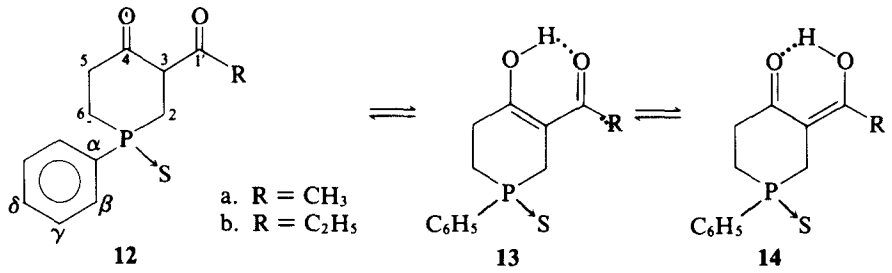
Enamine **1** in dry benzene was found to react with methyl vinyl ketone.[1] Interestingly, only one product was isolated and identified as **8.** Actually, **9, 10,** or **11** (from multiple alkylation) are not unreasonable products,[11] but apparently the CH_3CO_2H/-NaO_2CCH_3 combination used to hydrolyze the enamine was sufficient enough to catalyze the aldol-type ring closure and permit double bond migration to give the conjugated system **8.** IR analysis of **8** showed a band 1660 cm^{-1}, indicative of the presence of α,β-unsaturated carbonyl group.[1] These data also ruled out an isomer such as **10.** Furthermore, ^1H NMR analysis of **8** displayed a signal for a vinylic proton[12] at δ 5.97, but the remaining spectrum was quite complex since other protons resonances appeared as an envelop at δ 1.60–3.65.

^{13}C NMR analysis of **8** revealed signals for the carbons directly attached to phosphorus atoms [C(1) and C(3)] at 37.58 ppm [$^1J_{PC}$ = 51.46 Hz] and 31.34 ppm [$^1J_{PC}$ = 52.12 Hz], respectively. These were easily distinguished because of the large size of the coupling constants. Tentatively, we suggest that the former resonance is for C(1) due to the β-deshielding effect of the substituent at C(8a). Unsaturated carbonyl carbon C(6) and olefinic carbons C(5) and C(4a) appeared at 198.05, 126.32 and 161.46 [$^3J_{PC}$ = 5.99 Hz] ppm, respectively.[13] Although the signal for vinylic carbon C(4a) is somewhat downfield than might be expected, the ^{13}C resonance assignment is consistent with the size of the coupling constant and is reasonable considering a β-deshielding effect.[13] Interestingly, C(7) occurred at 34.98 ppm as a singlet. Moreover, only one ^{31}P NMR signal was observed for **8** at +33.43 ppm which supports one isomer.

Surprisingly, enamine **1** and mesityl oxide or 1-acetyl-1-cyclohexene[14] did *not* react and only starting material could be partially recovered (50–60%) along with some polymeric type substance. With longer reaction times and higher tempera-

tures, decomposition resulted. Steric factors may be important in reaction of enamine **1** with these unsaturated ketones.

Treatment of enamine **1** with freshly distilled acetic anhydride and/or propionic anhydride gave a solid product in each case.[1] These beta diketones **12a–b** were ob-



12 **13** **14**

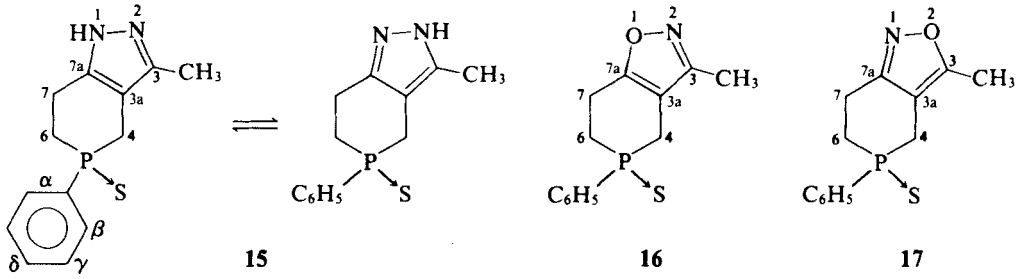
tained after hydrolysis in modest yields (39% and 35%). The ^{1}H NMR data (Experimental) showed that **12a** and **12b** had one signal each for the methyl protons at δ 2.12 and δ 1.08, respectively. The remaining pattern was complex in both cases.

The ^{13}C NMR spectrum of **12a** was not simple, and the interpretation was best in accord with a very high population of an enol form **13a** (or **14a**). For example, olefinic carbons C(3) and C(4) appeared at 101.99 ppm ($^2J_{PC}$ = 6.55 Hz) and 184.85 ppm ($^3J_{PC}$ = 10.30 Hz) for **13a** (or **14a**) and at 101.46 ppm ($^2J_{PC}$ = 5.93 Hz) and 183.04 ppm ($^3J_{PC}$ = 11.00 Hz) for **13b** (or **14b**), respectively.[15] Interestingly, ^{13}C NMR resonances for C(2) and C(6) in **13a** (or **14a**) appeared at 32.15 ppm ($^1J_{PC}$ = 52.42 Hz) and 27.93 ppm ($^1J_{PC}$ = 52.96 Hz).[16] As there is no close model system for comparison, we tentatively suggest that the latter resonance is for C(6). Carbonyl carbon [probably C(1′)] had a ^{13}C NMR signal at 195.45 ppm ($^3J_{PC}$ = 10.13 Hz).[16] Reasonably, the assignment was made for the C(5) resonance at 30.14 ppm ($^2J_{PC}$ = 6.58 Hz). For the ethyl compound **13b** (or **14b**), the assignments for the carbon signals parallel those found in **13a** (or **14a**) (Experimental). The ^{13}C resonances for the ethyl group in **13b** (or **14b**) appeared at 30.05 ppm and 8.37 ppm for the methylene and methyl carbons, respectively. No signals in the spectra of the compounds could be attributed to the diketo form **12a** or **12b** but rather only to **13a** (or **14a**) or **13b** (or **14b**).

Only one ^{31}P NMR signal was detected for each compound (**12a** and **12b**) at +31.87 ppm and +31.90 ppm (relative to 85% H_3PO_4), respectively. The ^{31}P NMR signal did not change for a solution of **13a** (or **14a**) in $DCCl_3$ at room temperature down to −70°C. In addition, IR analysis (on KBr pellets) of **12a** or **13a** and **12b** or **13b** revealed a broad band at 1587 cm^{-1} and 1600 cm^{-1}, respectively, which suggests a keto-enol mixture. The same keto-enol form is evident from ^{13}C NMR spectral data which shows that major tautomer in solution is **13** (or **14**) in both examples. Keto-enol tautomerism in C—P heterocycles is an area of activity.[3d,17].

Fused heterocycles in which one ring is a carbon-phosphorus unit are somewhat rare.[3a,3d,8] We have found that **12,** or rather the enol form **13** (or **14**), reacts with hydrazine and hydroxylamine hydrochloride to give phosphorinopyrazole **15** and a mixture of phosphorinoisoxazoles **16** and **17,** respectively, as indicated by ^{31}P NMR signals.[18–20] Unfortunately, TLC analysis of the isoxazoles revealed only one spot after attempted separation in three different solvent systems.

^{31}P NMR analysis of **15** showed a signal at +32.59 ppm (relative to 85% H_3PO_4). The ^{1}H NMR spectrum of **15** was quite complex, but a singlet for the methyl protons appeared at δ 2.22. The ^{13}C resonance for C(7) in **15** was assigned as 19.79 ppm



15 16 17

($^2J_{PC}$ = 6.58 Hz), based on the $^2J_{PC}$ coupling constant. Signals for the ring carbons attached to P → S [C(4) and C(6)] occurred at 29.06 ($^1J_{PC}$ = 52.88 Hz) and 27.99 ppm, ($^1J_{PC}$ = 50.97 Hz), respectively. Since there is no model system for comparison, we tentatively suggest that the former resonance is for C(4) which is also next to double bond.[16] Again olefinic carbon C(3a) at 106.60 ppm ($^2J_{PC}$ = 3.63 Hz) can be easily assigned due to chemical shift and coupling constant.[21] Only one ^{13}C NMR signal was visible for the methyl carbon at 10.42 ppm in **15**.

On condensation of **12a** (or **13a**) with hydroxylamine hydrochloride, a white crystalline material was isolated. In $DCCl_3$, this substance showed two ^{31}P signals at +30.65 and 31.90 ppm (relative to 85% H_3PO_4) in a ratio of 1:1.51. Two isomers like **16** and **17** have been detected in simple carbocyclic systems.[19,20] Moreover, ^1H NMR analysis of the mixture of **16** and **17** showed methyl singlets at δ 2.22 and δ 2.34. No change in the methyl signal was observed in the ^{31}P decoupled ^1H NMR spectrum which ruled out any possible phosphorus coupling with methyl group. Unfortunately, column chromatography of the mixture on silica gel did not prove fruitful to separate these isomers nor did several recrystallizations.

EXPERIMENTAL

Melting points were determined with a Thomas–Hoover capillary apparatus and were uncorrected. The ^1H, ^{13}C, and ^{31}P NMR data were obtained on a Varian XL-100(15) NMR spectrometer equipped with a Nicolet TT-100 PFT accessory operating at 100.1 MHz with tetramethylsilane (TMS) as internal standard for ^1H NMR, at 25.2 MHz (with TMS) for ^{13}C and at 40.5 MHz (with 85% H_3PO_4) for ^{31}P. The ^{13}C and ^{31}P NMR spectra were obtained operating in the FT mode utilizing broad-band proton decoupling. Multiplicity of the various signals was determined by off-resonance decoupling wherever it was possible. Infrared spectral data were collected on a Beckman IR-5A unit and mass spectral data were obtained on a CEC Model 21-110B HR mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

Starting Materials.

Reagents (commercially available) were purified before use where necessary. Solvents used were reagent grade and were dried over sodium where required. 1-Phenyl-4-phosphorinanone 1-sulfide (**2**) was prepared by the known procedure.[4]

Synthesis of 1-(1,2,3,6-Tetrahydro-1-phenyl-4-phosphorinyl)pyrrolidine P-Sulfide (1).

1-Phenyl-4-phosphorinanone 1-sulfide (**2**) (1.12 g, 0.005 mol)[4] was dissolved in 50 mL of dry C_6H_6. To this was added 0.88 g (0.0125 mol) of pyrrolidine and few crystals of PTSA. The mixture was boiled for 18–20 h under N_2 using a Dean-Stark apparatus to remove H_2O. Vacuum distillation (75–80°C/1mm) removed the solvent as well as the last traces of pyrrolidine. High vacuum distillation in a Kugelrohr apparatus at 190–195°C/0.025 mm gave a heavy yellow oil (accompanied by excessive decomposition as evidenced by tarring). Three separate runs gave an average yield of 32.5%. IR analysis of the enamine in

nujol did *not* show a peak at 1695 cm^{-1} (present in the IR spectrum of starting ketone **2**). It was noted that decomposition of enamine **1** occurred almost immediately upon exposure to the atmosphere or upon standing and therefore it was not possible to obtain a satisfactory elemental analysis. Thus, the apparently crude enamine was used as such without further purification.

4-Oxo-1-phenyl-3-phosphorinanepropionitrile 1-Sulfide **(3a).**

Crude enamine **1** was obtained from 1.12 g (0.005 mol) of phosphorinanone **2** and 0.88 g (0.0125 mol) of pyrrolidine as previously described. To the crude enamine dissolved in 25 mL of absolute C_2H_5OH was added 0.45 g (0.008 mol) of acrylonitrile and the resulting solution was boiled under N_2 for 36 h. The ethanol was evaporated and to the residue was added 10 mL of CH_3CO_2H at room temperature. This solution was boiled for another 20 h. After cooling, the new solution was extracted ($HCCl_3$; 3 × 25 mL portions). The extracts were washed with aq. $NaHCO_3$ (2%), then with H_2O and were then dried (Na_2SO_4). After filtration, the solution was concentrated to afford a dark brown liquid. This liquid was chromatographed over neutral alumina (40 g), elution being made with 350 mL of C_6H_6:$HCCl_3$ (1:1) to give a pale yellow liquid **3a** which solidified upon cooling. It was recrystallized (CH_3OH), mp, 99–100°C (0.9 g, 61%). Peak matching of the molecular ion gave: m/e 277.0690; found: 277.0694. IR (KBr) 2250, 1710, 1110 735 cm^{-1}. ^1H NMR($DCCl_3$) δ 1.50–3.75 [m, 11 H, H(2), H(3), H(5), H(6), H(7), H(8)], 7.40–7.70 [m, 3 H, Ar—H], 7.70–8.20 [m, 2 H, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz): C(2) *37.43* (49.83), C(3) *43.79* (4.81), C(4) *206.98* (5.27), C(5) *36.79* (5.87), C(6) *31.84* (52.09), C(7) *26.53* (13.91), C(8) 14.75, C(9) 118.88, C(α) *129.41* (80.88), C(β) *130.21* (10.86), C(γ) *128.59* (12.02), C(δ) *132.10* (2.91). ^{31}P NMR ($DCCl_3$) +33.13 ppm.

The thiosemicarbazone derivative **4** was prepared in the following manner. To a methanol solution (2 mL) containing 0.065 g (0.0007 mol) of thiosemicarbazide was added 2 mL of H_2O. This solution was added to ketone **3a** (0.175 g, 0.00063 mol) in CH_3OH (3 mL), and the reaction solution was warmed on a steam bath for 5 min. When the solution was cooled to room temperature, a solid precipitated was filtered out and recrystallized (CH_3OH) to give **4** as a white solid, mp 177°C (0.155 g, 70%).

Anal. Calcd. for $C_{15}H_{19}N_4PS_2$: N, 15.87; P, 8.85. Found: N, 16.00; P, 8.85. IR (KBr) 3340, 3225, 2222, 1587, 1477 cm^{-1}. ^1H NMR (DMSO-d_6) δ 1.50–3.80 [m, 11 H, H(2), H(3), H(5), H(6), H(7), H(8)], 7.20–7.70 [m, 3 H, Ar—H], 7.80–8.50 [m, 2 H, Ar—H]. ^{13}C NMR (DMSO-d_6) (partial assignments) *average* of doublets in ppm (J_{PC} in Hz): C(4) *152.73* (4.55), C(8) 14.42, C(9) 120.87, C(12) 179.14, C(α) *131.24* (78.61), C(β) *130.86* (9.57), C(γ) *128.70* (12.33), C(δ) *132.05* (3.52). ^{31}P NMR (DMSO-d_6) +29.24 ppm.

4-Oxo-1-phenyl-3-phosphorinanepropionic Acid 1-Sulfide **(3c).**

3-(β-Cyanoethyl)-1-phenyl-4-phosphorinanone 1-sulfide **(3a)** (0.70 g, 2.53 mmol) was dissolved in KOH solution (1.5 g in 10 mL of H_2O) and the resultant solution was boiled under N_2 for 36 h. After cooling, the reaction mixture was washed with $HCCl_3$ (3 × 10 mL) to remove neutral impurities. Then the reaction mixture was cooled (ice bath), and there was added, dropwise, concentrated HCl (6 mL) to bring the pH to 1–2. This solution was extracted with $HCCl_3$ (3 × 25 mL), and the extracts were washed (H_2O), dried (Na_2SO_4), and evaporated to give a thick yellow gum. This gum was dissolved in a minimum amount of $CH_3CO_2C_2H_5$ and, upon adding a few drops of petroleum ether (40–60°C), a light cream-colored, crystalline compound formed. Keto acid **3c** (0.46g; 62%) was recrystallized from $CH_3CO_2C_2H_5$: $HCCl_3$ (4:1), mp 163–163.5°C. Peak matching of the molecular ion gave: m/e 296.0634; found: 296.0634. IR (KBr) 3338, 1712, 1697, 1426 cm^{-1}. ^1H NMR (DMSO-d_6) δ 1.40–3.45 [m, 11 H, H(2), H(3), H(5), H(6), H(7), H(8)], 7.45–7.70 [m, 3 H, Ar—H], 7.80–8.35 [m, 2 H, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz): (partial assignments): C(4) *207.44* (5.29), C(9) 174.26, C(α) *131.00* (78.85), C(β) *130.96* (11.74), C(γ) *128.75* (12.43), C(δ) *132.12* (2.68). ^{31}P NMR ($DCCl_3$) + 27.95 ppm.

Octahydro-6-phenyl-2H-phosphorino[4,3-b]pyran-2-one 6-Sulfide (6).

Keto acid **3c** (0.098 g, 0.33 mmol) was dissolved in cold NaOH (1 N, 2.5 mL) and was treated with $NaBH_4$ (0.024 g, 6.6 mmol). The solution was stirred at room temperature for 2 days, cooled in ice, and acidified to pH-2 with concentrated HCl (~5 mL). After being stirred for 20 h, the solution was extracted (3 × 30 mL, $HCCl_3$). A gum formed and was dissolved in 50 mL of C_6H_6. To this was added 2–3 crystals of PTSA. This mixture was boiled for 4 h using a Dean–Stark water separator. The organic layer was washed with H_2O and then extracted with $HCCl_3$. The combined organic extracted were dried (Na_2SO_4) and evaporated to give a gum (0.06 g). This was dissolved in 5 mL of CH_3OH and stored over-

night at room temperature. The precipitated lactone **6** was filtered and dried to yield 0.024 g (26.1%), mp 166–166.5°C. Peak matching of the molecular ion gave: m/e 280.0687; found: 280.0688. IR (KBr) 1724, 1258, 1031, 687 cm^{-1}. ^1H NMR ($DCCl_3$) δ 1.50–3.05 [m, 11 H, H(3), H(4), H(4a), H(5), H(7), H(8)], 3.85–4.40 [m, 1 H, H(8a)], 7.40–7.70 [m, 3 H, Ar—H], 7.75–8.10 [m, 2 H, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz): C(2) 169.48, C(3) *33.32* (3.10), C(4) *29.77* (2.20), C(4a) *28.09* (6.02), C(5) *35.96* (50.70), C(7) *29.41* (44.03), C(8) *27.28* (5.19), C(8a) *82.30* (3.63), C(α) *130.92* (80.40), C(β) *130.37* (10.36), C(γ) *128.74* (11.87), C(δ) *132.07* (3.01). ^{31}P NMR ($DCCl_3$) + 33.75 ppm.

4-Oxo-1-phenyl-3-phosphorinanemethylpropionate 1-Sulfide **(7).**

Crude enamine **1** obtained from 1.12 g (5 mmol) of ketone **2** as previously outlined and 0.86 g (0.01 mol) of methyl acrylate were dissolved in 25 mL of absolute CH_3OH, and the solution was boiled under N_2 for 12 h. This was followed by the addition of 10 mL of H_2O, and the resulting solution was boiled for another 1 h. The solvent was removed (rotary evaporator), and the residual liquid was taken up in $HCCl_3$. The new organic solution was washed with 10% HCl (20 mL) and then with H_2O. Drying (Na_2SO_4) this solution and evaporation of the solvent gave a gum. Chromatography of the gum over silica gel using 300 mL of C_6H_6:$HCCl_3$ (1:1) gave ester **7** (0.825 g, 48.2%) as a yellow liquid. IR analysis showed an ester band (1727 cm^{-1}) and a carbonyl band (1706 cm^{-1}). Thus, a probable mixture of different isomers is present since ^{31}P NMR analysis also revealed five signals at +33.57, +33.02, +32.15, +31.54, and at +29.54 ppm. Upon further elution with 200 mL of $HCCl_3$:CH_3OH (20:1), there was recovered from the column a solid which was recrystallized from $CH_3CO_2C_2H_5$. The material melted at 164–164.5°C (0.18 g, 11.2%) and was shown by spectral analysis to be keto acid **3c** previously obtained from hydrolysis keto nitrile **3a.**

1,3,4,7,8,8a-Hexahydro-2-phenyl-6(2H)-isophosphinolinone 2-Sulfide **(8).**

Enamine **1** was prepared from 0.56 g (2.5 mmol) of ketone **2** as previously described and was dissolved in 40 mL of dry C_6H_6. To this was added, dropwise, 0.35 g (5 mmol) of methyl vinyl ketone while cooling (0°C) under N_2. This mixture was then boiled for 24 h. A buffer solution composed of 5 mL of CH_2CO_2H, 5 mL of H_2O and 2.5 g of CH_3CO_2Na was added to the reaction solution which was then boiled for 4 h. After washing with 10% HCl, and then with aqueous $NaHCO_3$ and finally with H_2O, the solution was dried (Na_2SO_4). Upon evaporation of the solvent, a gum formed which was chromatographed over silica gel and eluted with 400 mL of C_6H_6:$HCCl_3$ (1:1). A light yellow solid **8** (0.22%, 30%) was obtained and was recrystallized ($CH_3CO_2C_2H_5$); mp 168.5–169°C. Peak matching of the molecular ion gave: m/e 276.0737; found: 276.0738. IR (KBr) 1660, 1612, 1428, 885 cm^{-1}. ^1H NMR ($DCCl_3$) δ 1.60–3.65 [m, 11 H, H(1), H(3), H(4), H(7), H(8), H(8a)], 5.97 [s, 1 H H(5)], 7.35–7.70 [m 3 H, Ar—H], 7.75–8.25 [m 2 H, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz):C(1) *37.58* (51.46), C(3) *31.34* (52.12), C(4) *30.56* (5.30), C(4a) *161.46* (5.99), C(5) 126.32, C(6) 198.05, C(7) 34.98, C(8) *29.75* (14.51), C(8a)·*32.75* (3.96), C(α) *130.69* (79.50), C(β) *130.20* (9.29), C(γ) *128.52* (12.41), C(γ) *131.83* (2.81). ^{31}P NMR ($DCCl_3$) + 33.43 ppm.

3-(1'-Oxoethyl-1-phenyl-4-phosphorinanone 1-Sulfide **(13a).**

Enamine **1** was prepared from 0.56 g (2.5 mmol) of ketone **2** as discussed previously. Crude enamine **2,** dissolved in 25 mL of C_6H_6, was added dropwise to a solution of freshly distilled $(H_3COC)_2O$ (0.295 g, 2.6 mmol) in C_6H_6 (5 mL), and this solution was allowed to stand at room temperature for 1 h. It was then boiled for 10 h whereupon the solution turned to a dark brown color. Addition of 5 mL of H_2O, followed by boiling for 0.5 h, resulted in the solution becoming a light orange color. The organic layer was separated and the aqueous layer was extracted (3 × 25 mL, $HCCl_3$). The extracts and original organic layer were combined and washed with 5% HCl (10 mL) and finally with H_2O (10 mL). After drying (Na_2SO_4), the crude product was passed through silica gel and eluted with 300 mL of C_6H_6:$HCCl_3$ (1:1) to give a thick gum. This gum was dissolved in 5 mL of CH_3OH and stored at room temperature for 2 days. A very light cream-colored crystalline **13a** (or **14a**) formed (0.382 g, 39%); mp 95–95.5°C. Peak matching of the molecular ion gave: m/e 266.0528; found: 266.0528. IR (KBr) 3389, 1587, 823 cm^{-1}. ^1H NMR ($DCCl_3$) δ 2.12 [s, 3 H, CH_3], 2.25–3.45 [m, 7 H, H(2), H(3), H(5), H(6)], 7.30–7.65 [m, 3 H, Ar—H], 7.70–8.05 [m, 2 H, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz):C(2) *32.15* (52.42), C(3) *101.99* (6.55), C(4) *184.85* (10.30), C(5) *30.14* (6.58), C(6) *27.93* (52.96), C(1') *195.45* (10.13), CH_3 24.22, C(α) *131.53* (78.60), C(β) *130.23* (10.19), C(γ) *128.71* (11.82), C(δ) *131.93* (3.04). ^{31}P NMR ($DCCl_3$) + 31.87 ppm.

3-(1'-Oxopropyl-1-phenyl-4-phosphorinanone 1-Sulfide **(13b).**

To enamine **1**, prepared from 0.15 g (0.66 mmol) of ketone **2** and dissolved in 25 mL of C_6H_6, was added 0.085 g (0.66 mmol) of freshly distilled propionic anhydride. After the usual workup as previously described, a thick gum was obtained. This gum was chromatographed over silica gel and eluted with C_6H_6:$HCCl_3$ (1:1) 300 mL. A light yellow gum isolated was cooled in dry ice and 5 mL of petroleum ether (36–50°C) was added. A very light yellow product **13b** (or **14b**) was obtained and recrystallized (H_3COH) (0.065 g, 35%); mp 92–92.5°C.

Anal. Calcd. for $C_{14}H_{17}O_2PS$: C, 59.85; H, 6.20; P, 11.23; S, 11.36. Found: C, 60.00; H, 6.07; P, 11.07; S, 11.43. IR (KBr) 1600, 1185, 823, 740 cm^{-1}. ^1H NMR ($DCCl_3$) δ 1.08 [t, 3 H, CH_2–CH_3], 2.05–3.45 [m, 9 H, H(2), H(3), H(5), H(6), CH_2–CH_3], 7.35–8.15 [m, 5 H, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz):C(2) *31.49* (50.87), C(3) *101.46* (5.93), C(4) *183.04* (11.00), C(5) *29.74* (6.60), C(6) *28.40* (53.00), C(1') *199.67* (9.53), CH_2CH_3 30.05, CH_2CH_3 8.37, C(α) *131.60 (78.64), C(β) 130.27* (9.80), C(γ) *128.68* (11.83). ^{31}P NMR ($DCCl_3$) + 31.90 ppm.

4,5,6,7-Tetrahydro-3-methyl-5-phenyl-1H-phosphorino[4,3-c]pyrazole 5-Sulfide **(15).**

Diketone **13a** (or **14a**) (0.1 g, 0.38 mmol) in 5 mL of anhydrous H_3COH (freshly distilled from Mg) and 0.091 g (3.8 mmol) of hydrazine were stirred and boiled (under N_2) for 3.5 h. After addition of 3 mL of H_2O, the solution was heated for 20 min and then cooled in a refrigerator (2 h) to give white crystalline **15.** This product was recrystallized (H_3COH) (61 mg; 62%); mp 95–96°C. Peak matching of the molecular ion gave: m/e 262.0693; found: 262.0691. IR (KBr) 3400, 3300, 1440, 1110 cm^{-1}. ^1H NMR ($DCCl_3$) δ 2.22 [s, 3 H, CH_3], 2.25–3.75 [m, 7 H, H(4), H(6), H(7), NH], 7.30–7.60 [m, 3 H, Ar—H], 7.65–8.15 [m, 2 H, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz):C(3) *142.14* (8.00)†, C(3a) *106.60* (3.63), C(4) *29.06* (52.88), C(6) *27.99* (50.97), C(7) *19.79* (6.58), C(7a) *141.49* (2.74)†, CH_3 10.42, C(α) *131.48* (78.00), C(β) *130.30* (9.84), C(γ) *128.59* (11.86), C(δ) *131.68* (2.22). ^{31}P NMR ($DCCl_3$) + 32.59 ppm.

Interestingly, the corresponding N—CH_3 [In place of the $C_6H_5P(S)$ group] had the following ^1H NMR data: δ 5.81 ($DCCl_3$) for the vinylic proton; IR (film) 1670 (C=O) and 1626 (C=C) cm^{-1}; see N. Finch, L. Blanchard, R. T. Puckett and L. Werner *J. Org. Chem.* **39,** 1118 (1974).

4,5,6,7-Tetrahydro-3-methyl-5-phenylphosphorino[3,4-d]isoxazole 5-Sulfide and 4,5,6,7-Tetrahydro-3-methyl 5-phenylphosphorino[4,3-c]isoxazole 5-Sulfide **(16 and 17).**

A mixture of ketone **13a** (or **14a**) (0.1 g, 0.38 mmol) and 3 mL of glacial H_3CCO_2H was placed in a dry flask (under N_2). Hydroxylamine hydrochloride (0.1 g, 1.44 mmol) and H_3CCO_2Na (0.25 g, 1.84 mmol) were dissolved in 0.5 mL of H_2O and added to the reaction flask. The resulting solution was heated in 100°C for 1 h (oil bath) and then allowed to cool to room temperature and 3 mL of H_2O was then added. This mixture was extracted (3 × 15 mL, $HCCl_3$) and the extracts were dried (Na_2SO_4). Evaporation of the solvent gave a solid mass which was recrystallized (H_3COH)(54 mg, 54.6%); mp 97.5–99.5°C. Peak matching of the molecular ion gave: m/e 263.0533; found: 263.0529. IR (KBr) 1435, 1110 cm^{-1}. ^1H NMR($DCCl_3$) δ 2.15–3.60 [m, ring CH_2], 2.22 and 2.34 [2 s, 2 CH_3], 7.45–8.05 [m, Ar—H]. ^{13}C NMR ($DCCl_3$) *average* of doublets in ppm (J_{PC} in Hz):C(3a) *105.11* (5.79), *106.86* (5.88), C(4) *27.14* (51.28), *28.05* (52.80), C(6) *27.21* (52.30), *28.39* (52.86), C(7) *18.58* (6.46), *19.86* (6.48), C(7a) *157.65* (11.11), *164.83* (15.40), CH_3 9.81, 11.00. ^{31}P NMR ($DCCl_3$) + 30.65 and +31.90 ppm [ratio of 1:1.51, respectively].

The Ar—C could not be assigned unequivocally and C(3) overlapped with the ^{13}C signals for the aromatic carbons.

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† Signals may be reversed.

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